Neck of Humerus Fractures: Epidemiology, Predictors of Nonunion and Classification

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Declaration

This thesis and its composition are entirely my own work. I have carried out the work described here, under the supervision of Mr Mike Robinson, Prof Hamish Simpson and Mr Tim White. The contributions and assistance of others in data collection and analysis have been appropriately acknowledged. I have not submitted the work in candidature for any other degree, diploma or professional qualification.

Ewan B Goudie

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Abstract

Proximal humerus fractures are common, accounting for 5% of fractures to the appendicular skeleton. Neck of humerus fractures (NHF) account for approximately 80% of all fractures of the proximal humerus – the remainder being isolated fractures of the greater, or lesser tuberosity. NHF should be considered as a separate entity to isolated tuberosity fracture as both injuries have distinct epidemiological characteristics, natural history and treatment principles. Despite this, many of the studies which form the basis for our understanding of NHF are in series which include all proximal humerus fractures.

There are important unanswered questions regarding the epidemiology and determinants of outcome of NHF, and no robust evidence base to guide their management. Furthermore, there is no existing fracture classification system that is of proven value in predicting outcome. As a consequence, patients with similar injuries may receive very different opinions about the severity of their fracture, its likely prognosis, and its best treatment, dependent on the unit in which they are treated and the surgeon who treats them. This thesis aims to investigate the epidemiology of NHF, identify the prevalence and risk factors for nonunion and develop and evaluate a novel fracture classification.

In CHAPTER 2 the study setting and method of case ascertainment was described. In CHAPTER 3 and CHAPTER 4, a large prospective database of 2,368 fractures collected over 7 years was used to define the epidemiology of NHF. Radiographs for these factures were analysed and the prevalence of nonunion was

determined. Multiple logistic regression analysis of the data was performed to identify those radiographic factors that are prognostic of nonunion. The statistical method used provided weighted significance for each of those factors, and thus a mathematical formula predictive of nonunion was constructed. In CHAPTER 5 a novel classification for NHF based on clinically relevant fracture patterns and radiographic predictors of nonunion was described. In CHAPTER 6 and CHAPTER 7 a second database of 419 fractures collected over a one-year period was used to prospectively to evaluate the novel fracture classification as well as the mathematical formula's ability to predict nonunion.

NHF occurred predominantly in the older female patient following a simple fall. The prevalence of nonunion was 7.1%. Worsening social deprivation and cigarette smoking were the patient factors associated with nonunion. The radiographic predictors of nonunion were increasing humeral head-shaft translation, increasing varus angulation of the humeral head, separation at the fracture and absence of an associated tuberosity fracture. A mathematical formula for predicating nonunion was developed based on these risk factors. The formula performed well when evaluated on a second prospectively collected dataset. A novel fracture classification was described based on clinically relevant fracture patterns and the radiographic predictors of nonunion. The majority of fractures had a 'stable' configuration according to the novel classification. Fractures with a 'stable' configuration had a very low rate of nonunion and fractures with an 'unstable' configuration had a higher rate of nonunion.

In summary, the prevalence of nonunion after NHF has been established. Risk factors for nonunion have been identified and a predictive formula has been developed which could improve patient counselling and decision making in fracture management.

A novel prognostic fracture classification has been introduced which could facilitate better comparison between individual fracture subtypes in future studies.

Lay Summary

Shoulder fractures involving the neck of the humerus (NHF) are commonly treated injuries by orthopaedic surgeons. Despite this, there are important unanswered questions regarding the characteristics of patients sustaining these injuries, the determinants of outcome, and there is no robust evidence base to guide management. Furthermore, there is no existing fracture classification system that is of proven value in predicting outcome. As a consequence, patients with similar injuries may receive very different opinions about the severity of their fracture and its best treatment, dependent on where they are treated and the surgeon who treats them. This thesis aims to investigate the characteristics of patients with NHF, identify risk factors for poor outcomes and develop and evaluate a new fracture classification.

A database of 2,368 fractures collected over 7 years was used to define the characteristics of patients with NHF. Radiographs for these fractures were analysed to determine how often fractures failed to heal and risk factors for fractures failing to heal were established. A new classification based on radiographs was described. A second database of 419 fractures collected over a one-year period was used to evaluate the new fracture classification.

NHF occurred predominantly in the older female patient following simple falls. The risk of a fracture failing to heal was 7.1%. Patients who smoked cigarettes were at increased risk of their fractures failing to heal. Four radiographic risk factors for fractures failing to heal were identified and formed the basis of new fracture

classification for NHF which might facilitate better comparison between individual fracture subtypes in future studies.

Ethics Statement

South East Scotland Research Ethics Service

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Dear Ewan,

Project Title: Outcome following proximal humerus fractures

You have sought advice from the South East Scotland Research Ethics Service on the above project. This has been considered by the Scientific Officer and you are advised that, based on the submitted documentation (email correspondence and Outcome following proximal humerus fractures), it does not need NHS ethical review under the terms of the Governance Arrangements for Research Ethics Committees (A Harmonised Edition).

The advice is based on the following:

- *The project is an evlauation limited to using data obtained as part of usual care, but note the requirement for Caldicott Guardian approval for the use or transfer of person-identifiable information within or from an organisation*

- *The project is a survey seeking the views of NHS patients on service delivery*

If the project is considered to be health-related research you will require a sponsor and ethical approval as outlined in The Research Governance Framework for Health and Community Care. You may wish to contact your employer or professional body to arrange this. You may also require NHS management permission (R&D approval). You should contact the relevant NHS R&D departments to organise this.

For projects that are not research and will be conducted within the NHS you should contact the relevant local clinical governance team who will inform you of the relevant governance procedures required before the project commences.

This letter should not be interpreted as giving a form of ethical approval or any endorsement of the project, but it may be provided to a journal or other body as evidence that NHS ethical approval is not required. However, if you, your sponsor/funder feels that the project requires ethical review by an NHS REC, please write setting out your reasons and we will be pleased to consider further. You should retain a copy of this letter with your project file as evidence that you have sought advice from the South East Scotland Research Ethics Service.

Yours sincerely,

Alex Bailey
Scientific Officer
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INVESTORS IN PEOPLE Healthy Working Lives 1

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CHAPTER 1
INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

This thesis describes a series of studies which investigate epidemiological and clinical aspects of fracture of the neck of humerus (NHF). A novel fracture classification is introduced and evaluated.

NHF accounts for approximately 80% of all fractures of the proximal humerus – the remainder being isolated fractures of the greater, or lesser tuberosity(1). NHF should be considered as a separate entity to isolated tuberosity fracture as both injuries have distinct epidemiological characteristics, natural history and treatment principles. Despite this, many of the studies which form the basis for our understanding of NHF are in series which include all proximal humerus fractures(1-3). It is therefore important to note that (for the most part) the literature reviewed below relates to all proximal humerus fractures rather than specifically NHF which is the focus of this thesis.

Proximal humerus fractures are common, accounting for 5% of fractures to the appendicular skeleton(1). The majority of NHF are stable, minimally-displaced, osteoporotic fractures in frail, elderly patients and are the result of low energy falls. Most patients with these injuries will regain a pain free, functional shoulder without operation.

However, a minority are more complex, displaced multipart fractures some of which are at increased risk of nonunion and poor functional outcome. Patients with NHF are thus a heterogeneous group with varying prognosis and treatment requirements. There are important unanswered questions regarding the epidemiology and determinants of outcome of these injuries, and no robust evidence base to guide their management. Furthermore, there is no existing fracture classification system that is of proven value in predicting outcome. As a consequence, patients with similar injuries may receive very different opinions about the severity of their fracture, its likely prognosis, and its best treatment, dependent on the unit in which they are treated and the surgeon who treats them.

An understanding of the anatomy of the proximal humerus and adjacent structures, the mechanism of injury, pathoanatomy, epidemiology and existing classification systems for NHF is a prerequisite to any investigation designed to address these uncertainties.

1.2 CLINICAL ANATOMY

The normal anatomy of the proximal humerus is considered first in this chapter and is based on an account provided in Rockwood and Green's Fractures in Adults(4).

1.2.1 **Bone**

The proximal humerus comprises, by definition, the anatomical regions of the metaphysis and epiphysis. This consists of the humeral head, the greater and lesser tuberosities and the proximal humeral metaphysis. The anatomic neck is just above the tuberosities in the region of transition between the articular cartilage of the humeral head and the surrounding bone. The region immediately inferior to the tuberosities at the metaphyseal flare of the proximal humerus is the surgical neck. The calcar is the posteromedial metaphyseal bone between anatomical neck and the proximal humeral shaft.

The articular surface of the humeral head occupies approximately one third of a sphere, with a radius of curvature averaging 25mm (with a range of 23 to 29mm)(5). The inclination of the humeral head in relation to the shaft averages 130 degrees (with a range of 123 to 136 degrees), and the geometric centre of the humeral head is offset an average of 2.6mm posteriorly (with a range of -0.8 to 6.1mm) and 7mm (with a range of 3 to 11mm) medially from the axis of the humeral shaft(6-8) (Figure 1-1). In the axial plane, the posterior angle of the anatomic neck of the humerus with relation to the epicondylar axis averages 17 degrees however the version may vary from between 5 degrees of anteversion to 50 degrees of retroversion(9, 10) (Figure 1-1).

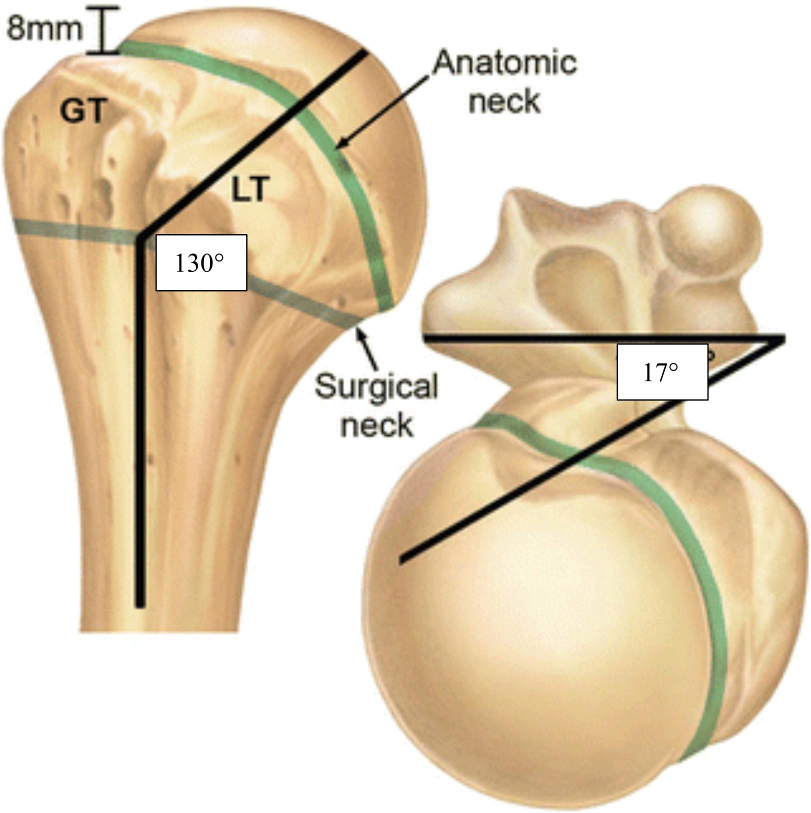


Figure 1-1 Diagram showing the normal anatomy of the proximal humerus. The inclination of the humeral head in relation to the shaft averages 130 degrees and the posterior angle of the anatomic neck of the humerus with relation to the epicondylar axis averages 17 degrees.

The distribution of bone within the proximal humerus is not uniform. The subchondral bone beneath the articular surface is dense cancellous bone, with bone mineral density decreasing progressively toward the geometric centre of the humeral head and into the metaphyseal area of the surgical neck(11). The head is therefore analogous to a hen's egg with a strong, compression resistant exterior and a less mechanically robust interior(12-14).

The greater tuberosity lies laterally on the proximal humerus and is the insertion point for the supraspinatus tendon superiorly, the infraspinatus tendon posterosuperiorly and the teres minor tendon posteriorly(15). The greater tuberosity is on average 9mm distal to the most proximal aspect of the humeral head (with a range of 6 to 10mm)(15).

The lesser tuberosity is situated on the anterior aspect of the proximal humerus and is the insertion site of the subscapularis tendon. The lesser and greater tuberosites are separated by the bicipital groove, which serves as the track for the long head of biceps. The bone surrounding the bicipital groove is strong cortical bone and is therefore only fractured in cases of high energy trauma or severe osteopenia. It is therefore a useful landmark for fracture reduction(16).

1.2.2 **Soft tissue**

Several muscles play a key role in proximal humerus fractures. The rotator cuff muscles cause displacement of the proximal fracture segment whereas the pectoralis major is responsible for displacing the shaft segment. The rotator cuff is composed of the subscapularis anteriorly, the supraspinatus superiorly and the infraspinatus and teres minor posteriorly(15).

When fractured, the greater tuberosity is typically pulled medially, superiorly and posteriorly by supraspinatus, infraspinatus and teres minor, whilst the lesser tuberosity is displaced anteriorly and medially by subscapularis. The pull of the rotator cuff muscles on the tuberosity attachments also explains why the humeral head is usually rotated posteriorly in a fracture involving the humeral neck and greater tuberosity as a result of the unopposed pull of subscapularis(4). Fracture of a tuberosity fragment defunctions the rotator cuff muscles that attach to it, and the tendon will regain function only once the fracture has healed. A tuberosity fragment that becomes displaced and heals in a malunion may produce longer-term dysfunction of the attached tendons or may give rise to subacromial or coracoid impingement(8, 17, 18).

1.2.3 **Vascular**

Perfusion of the intact proximal humerus is from the axillary artery where it passes between the pectoralis minor and teres major muscles(19). At this level, the axillary artery gives off the anterior and posterior circumflex humeral arteries which anastamose medially in the quadrilateral space, laterally in the area of the greater tuberosity, and in the humeral head through the rich network of interosseous anastamoses(20). Osteonecrosis of the humeral head due to vascular injury is a rare complication of NHF.

1.3 PATHOMECHANISM OF INJURY

The vast majority of proximal humerus fractures occur in elderly patients and are usually low energy, osteoporotic injuries(1, 21-23). More than three quarters follow domestic falls and the risk of fracture is associated with low bone mineral density(1, 23, 24). Fractures in younger adults are less common and usually occur due to high energy injuries, often from road traffic accidents, sporting injuries or falls from height(1).

A proximal humerus fracture may occur from direct impact to the shoulder or indirectly by transmission of forces from a fall onto the outstretched arm. The neck of humerus is thought to fracture on the hard-packed bone of the glenoid which acts as an anvil during impact on the shoulder(25). The interaction of this external force with the forces generated by the intrinsic shoulder musculature, and the quality of the humeral bone stock, determines the initial fracture configuration and any ensuing displacement(25, 26). In some cases the humeral head may remain neutral, but often there is either varus or valgus angulation.

1.3.1 **Varus fractures**

The pathomechanism of varus fractures was described by Edleson in a combined study of fracture specimens and three-dimensional CT reconstructions in 2004(25). The following section is a summary of this original description.

Impaction with the glenoid results in compressive loading of the humeral head and bending forces at the surgical neck(25). Often, the proximal humerus epiphysis is able to resist these forces but the weaker metaphysis fails, resulting in an isolated surgical neck fracture. The glenoid drives the head backwards because of the position of internal rotation in which the fall usually takes place augmented by normal retroversion of the head. The principal deformity is backward and downward tilting of the head on the shaft. The major fracture line is through the relatively weak metaphyseal bone of the surgical neck with comminution and impaction to the posteromedial aspect of the shaft inside the head. The backward tilt may give rise to the impression of an exaggerated valgus of the head when seen on a standard anteroposterior (AP) radiograph, especially if taken in internal rotation, the posture in which a patient's arm is commonly immobilised. This is a similar concept to the altered AP radiographic appearance of the proximal humerus due to fixed internal rotation that is seen following a posterior shoulder dislocation. However, the humeral head actually rotates into varus, especially when there is substantial comminution in the calcar resulting in loss of the medial support of the head.

In some cases, the epiphyseal bone may fracture in addition to the surgical neck, leading to more complex, multifragmentary fractures involving the greater and or the lesser tuberosities. A similar pattern of forceful backward tilting of the fragment of the head is seen but it can be more difficult to detect because of the overlapping and distortion of the numerous bone fragments.

1.3.2 **Valgus fractures**

Robinson described the pathomechanism of the spectrum of sub-types for valgus impacted proximal humeral fractures(27). The following section is a summary of this original description.

During a fall the humeral head and glenoid are driven together by an axial loading force. The interaction of this external force with the internal forces generated by the intrinsic shoulder musculature creates the initial fracture configuration and any ensuing displacement. In a valgus fracture, the head hinges around the inferomedial aspect of the stronger calcar bone(27). If the deforming force transferred to the proximal humerus is relatively minor, the degree of displacement of the humeral head is slight, causing a secondary fracture of the greater tuberosity (and, also, rarely of the lesser tuberosity). The tuberosity fracture is usually the most striking feature on the initial trauma series radiographs. Many of these fractures are, therefore, misdiagnosed as isolated greater tuberosity fractures, and occasionally the anatomic neck fracture cannot be seen without further specialist imaging.

When a greater axial loading force is applied, or if the proximal humerus is more osteoporotic, the humeral head is pushed into the metaphysis causing increasing amounts of valgus impaction(25). The intact periosteal hinge between the humeral head and the medial calcar is the axis around which the humeral head pivots as it is displaced. There are 3 key anatomic features of this injury. First, the greater tuberosity is pushed laterally and fractured by the impaction of the humeral head into the metaphysis. Usually, the fracture line passes just posterior to the bicipital groove splaying the tuberosities apart, with the head fragment situated between them(27). Alternatively, if the fractured tuberosities remain attached to each other, they form a larger composite “shield” fragment, which acts as an obstacle to open operative reduction. In both injury patterns, if the humeral head is less displaced, the tuberosities usually retain some periosteal attachments to the shaft and severe or progressive displacement of these fragments is, therefore, unusual. Second, the force applied to the head by the glenoid in valgus impacted fractures may not always be directed axially. Instead, possibly due to variability of arm position at the time of injury and retroversion of the head, dorsal tilt of the head can occur, creating a posterior fracture-subluxation(28). In these cases, the dorsomedial periosteum may potentially remain intact, despite more significant posterolateral displacement of the head. These injuries are often erroneously described as posterior fracture-dislocations, a term which is best reserved for the more uncommon situation where the humeral head is completely extruded from the soft-tissue envelope and is engaged on the posterior glenoid rim(29). Third, as the larger surface area of the humeral head impacts against the narrow “anvil” of the glenoid, it is unusual for the articular surface of the humeral head to be completely intact. Significant marginally impacted portions of the articular surface may be completely loose or are more commonly attached to the fractured tuberosities.

1.4 EPIDEMIOLOGY

As noted above our understanding of the epidemiology of NHF is based on studies which have considered all proximal humerus fractures, i.e. isolated tuberosity fractures as well as those involving the humeral neck(1). According to this definition proximal humerus fractures are the most common fractures affecting the shoulder girdle with an overall annual incidence of between 63 and 105 fractures per 100,000 population per year(1, 2, 21). They account for 5% of fractures to the appendicular skeleton(2).

Proximal humerus fractures follow a unimodal elderly distribution(1, 30).There is a low incidence under the age of 40 years and an exponential increase thereafter(31). Most fractures occur between the ages of 65 and 75 years however, due to the skewed population demographic the age/sex adjusted incidence in the elderly is much higher. There are marked gender differences with 70 to 80% of fractures occurring in women(1, 31-33). Men who present with proximal humerus fractures are on average 8 to 10 years younger than women and this is mostly likely due to differences in the distribution of mechanism of injury between the two genders(34). Most fractures in women occur after low energy falls, whereas the rates of sporting injuries and road traffic accidents, typically occurring at a younger age are higher in men(35). Additionally, isolated tuberosity fractures tend to occur in patients who are on average 10 to 15 years younger than patients sustaining NHF and are relatively more common in men(36).

Patients who present with proximal humeral fractures have a higher pre injury level of function than those who present with proximal femoral fractures but a lower pre injury level of function than those having distal radial fractures(32). In one series fewer than 10% of patients presenting with proximal humerus fractures were institutionalised and about two-thirds of the group lived by themselves, with less than one-fifth requiring social support(1). There is one study on epidemiology of proximal humerus fractures and social deprivation which demonstrated an increased fracture incidence with higher levels of deprivation(37).

1.5 CLASSIFICATION

1.5.1 Historical background

As early as the late 19th century efforts were made to classify proximal humerus fractures. Kocher first divided proximal humerus fractures into supratubercular, pertubercular, infratubercular, and subtubercular(38). In 1934, Codman recognised that the proximal humerus tends to fracture along its physeal lines of fusion into four principal fragments (the articular surface, humeral shaft, greater tuberosity, and lesser tuberosity)(39). Subsequent classification schemes focused on mechanism of injury such as the Watson- Jones' classification, which described impacted adduction, impacted abduction, and a minimally displaced 'contusion-crack' fracture(40). Dehne felt that forced abduction separated the head, greater tuberosity, and shaft from one another, leading to a 'three-fragment fracture'(41). Forced extension, on the other hand, separated the surgical neck from the shaft into a 'two fragment fracture', while the 'head-splitting fracture' resulted from the head being driven into the glenoid.

In 1950 De Anquin and De Anquin proposed a classification that divided the proximal humerus into three zones and fracture fragments(42). They noted a difference between impacted and non-impacted four-part fractures(42). Depalma differentiated between fracture dislocations with complete loss of articular contact and rotational deformities (where the head remained in the joint capsule despite being spun)(43).

In 1970 Neer refined Codman's idea of four possible fracture fragments to produce the classification that remains most widely used today(44). This system was based on an observational study of 300 displaced proximal humerus fractures. Each of the four fragments (the articular surface, humeral shaft, greater tuberosity, and lesser tuberosity) are considered as unique parts only if they are separated by more than 1cm or angulated by more the 45 degrees to one another.

Developed in the 1980s, the AO/OTA classification was an attempt to make a classification system that was inclusive of all fracture types(45). The system included 27 subtypes distinguished by articular surface involvement, location and degree of comminution and dislocation. An important distinction is made between valgus-impacted four-part fractures and the classic four-part fracture described by Neer(44). Although the AO/OTA classification provides a comprehensive method of describing proximal humerus fractures, it is complex and not intuitive which reduces its usefulness. When divided into nine groups, intraobserver reliability and interobserver reproducibility were only moderate, with mean kappa coefficients of 0.48 and 0.42 respectively(46). The addition of CT scanning did not improve these values(47, 48). For these reasons, whilst this system has been retained by the Orthopaedic Trauma Association in its recent fracture compendium, it is seldom used in either clinical practice or in the academic literature(49).

More recently other classifications have been produced but none has proved as robust over time or gained the general acceptance of the Neer classification(25, 47, 50-52). The following sections discuss the Neer classification in more detail and consider the additional value and limitations of more recently described classifications.

1.5.2 **The Neer classification**

Fractures of less than 1cm of displacement and less than 45 degrees of angulation are described as one-part. Neer's concept is that one part fractures behave similarly regardless of their fracture lines. Displaced fractures take their name from the number of displaced segments and the key segment that displaces. Two-part fractures are named after the segment that displaces, the most common of which is the two-part surgical neck fracture in which the tuberosities remain attached to the head fragment. Two-part surgical neck fractures typically exhibit apex anterior angulation of the shaft. Isolated greater tuberosity fractures displace posteromedially by the unopposed pull of the supraspinatus and infraspinatus tendons. Isolated lesser tuberosity fractures are very uncommon and displaced medially by the pull of the subscapularis tendon. Three-part fractures tend to be fractures of the surgical neck accompanied by the greater tuberosity or less commonly the lesser tuberosity. In three-part greater tuberosity fractures the head is rotated posteriorly by the action of the subscapularis muscle via the intact lesser tuberosity. Four-part fractures exhibit displacement of all segments. Fracture dislocations are classified by the direction of dislocation, number of segments and whether the articular surface is involved.

Despite its widespread use, the Neer classification has several shortcomings. Kristiansen et al found poor intraobserver reliability, especially amongst inexperienced observers(53). Categorisation was based on only AP and lateral radiographs rather than a complete trauma series. Interobserver reproducibility was not measured and a condensed version of the classification was used. Sidor et al. showed a reliability coefficient of 0.5 for their evaluation of 50 fractures by observers of different experience levels(54). Intraobserver reliability was highest for the shoulder specialist at 0.83 and lowest for the skeletal radiologist at 0.5. Siebenrock and Gerber found a mean kappa value of 0.4 and 0.6 for interobserver and intraobserver reliability, respectively(46). Additionally, advances in imaging technology have permitted a better understanding of pathoanatomic factors that may be associated with prognosis which are not accounted for in the Neer classification.

1.5.3 **Modern fracture classifications**

In 2004, Hertel devised a binary system to classify proximal humerus fractures as part of an attempt to predict which fractures were at risk for development of avascular necrosis(50). Based on the location of five possible fracture lines there were 12 basic fracture types identified. LEGO blocks were used to help pictorially represent the 12 fracture types and each type of fracture was assigned a number. A fracture fragment was considered to be present if a cortical disruption could be identified on any radiographic view. Hertel studied 100 intracapsular fractures undergoing operative treatment. He identified distal metaphyseal extension of the head fragment of 8mm or less, disruption of the medial hinge between the humeral head and the shaft at the level of the calcar and fractures of the anatomic neck to be independent predictors of humeral head ischaemia. Although this study been widely used to help decision making in the treatment of proximal humerus fractures, a follow-up study from the same authors found a poor correlation between intraoperative ischaemia and the development of avascular necrosis(55). This discrepancy is supported by a more recent study in which tetracycline was administered to patients prior to undergoing hemiarthroplasty for proximal humerus fractures. Humeral head specimens were obtained from the surgery and analysed sing fluoroscopic microscopy. Fluorescence was observed in all specimens suggesting that vascular supply was not disrupted in any of the fracture patterns(56).

The authors of the HGLS system felt that while the binary LEGO system was a good classification scheme, its numbering system was confusing and led to errors in correctly categorizing fractures and decreased reliability(57). They introduced an alphabet-based ‘pictogram’ to use in description of fractures that they felt simplified classification.

Through a combined study of museum specimens, 3DCT scans, and observation at the time of surgery, Edelson attempted to relate mechanism of injury with pattern of bony displacement and introduced the concept of varus and valgus malpostion of the head fragment(25). Varus and valgus malposition are associated with a different pattern of periosteal damage, different primary stability, different ways of fracture reduction, and different functional outcome(58-62).

In another CT study, Mora Guix developed an image reading protocol based on 21 proximal humerus fracture characteristics - including fracture impaction, displacement between the humeral head and shaft, angulation of the head fragment and tuberosity involvement(63). Whist this provides detailed description of fracture pathoantomy, it is impractical to apply this complex CT protocol to everyday clinical practice.

In 2011, Resch, suggested that fracture impaction and angulation in both the coronal and sagittal planes were important fracture characteristics(47). Subsequently, he described five characteristic fracture patterns based on 3DCT analysis(52). Nondisplaced fractures were classified as type 1, fractures with normal coronal head position but sagittal deformity as type 2, valgus fractures as type 3, varus fractures as type 4 and fracture dislocations as type 5. Each fracture was further classified in terms of greater or lesser tuberosity involvement.

All of these studies have improved our understanding of proximal humerus fracture pathoanotomy however none have produced an adequate fracture classification system. Their use is limited by relying on 3DCT scanning which is not routinely performed in the majority of patients with proximal humerus fractures and none of them describe the full spectrum of injuries commonly encountered in clinical practice. None of them have been shown to predict nonunion.

1.5.4 **Population based studies of proximal humerus fracture pattern**

Several studies have reported population based data in relation to fracture pattern(1, 36, 64). In the earliest population based study, published in 2001, a total of 1,027 fractures were classified over a 5 year period using both the Neer and AO systems(1, 44, 65). Based on Neer undisplaced or minimally displaced one-part fractures comprised half (49%) of all fractures. Two-part fractures represented 37% of the cohort. Three part fractures occurred in 10% of patients, almost all of which involved the neck of humerus and the greater tuberosity. Complex four-part fractures accounted for the remaining 3% of the group. The incidence of more complex fractures increased with age. Based on the AO system, the commonest single fracture configuration seen during the study period was the impacted valgus fracture B1.1. This accounted for 15% of all proximal humeral fractures. It is of note that this type is not included in the Neer classification. A further three fracture configurations had an incidence of at least 10%, these being the impacted varus surgical neck fracture (A2.2), the translated surgical neck fracture (A3.2) and the displaced surgical neck fracture the (A1.2). Ten of the 27 different sub-groups listed in the AO classification had an incidence of less than 1%.

Based on these observations the authors concluded that the literature does not adequately reflect the spectrum of proximal humerus fractures.

A more recent study described the epidemiology of fractures according to the AO system using data from the Swedish Fracture Registry(36). This examined 1,582 proximal humerus fractures over a two year period. In this series 16.5% of fractures were isolated greater tuberosity fractures (11-A1). 28.4% of fractures involved the neck of humerus only of which approximately two thirds were impacted metaphyseal fractures (11-A2) and one third were non-impacted (11-A3). 9.2 percent of fractures were valgus impacted (11-C1 and 11-C2). 42.4% involved the neck and either one or both tuberosities but without valgus impaction (11-B1 and 11-B2). The remaining 3.4% (11-B3 and 11-C3) were fracture dislocation. No correlation was found between mechanism of injury and AO type.

Bahr’s 2014 retrospective review of hospital registry data from a transregional level 1 trauma centre in Tubingen, Germany describes a series of 815 fractures in patients treated during 5 year period(64). This series does not include 192 undisplaced and minimally displaced proximal humeral fractures in adult patients from the hospital catchment who were treated nonoperatively by local privately practicing surgeons. Fractures were categorised according to the AO and Neer classifications and then within each classification arranged in 4 predefined groups of ascending complexity (1 to 4). Based on the Neer classification, 113 (13.9 %) were minimally displaced proximal humeral fractures (fracture-complexity group 1). The authors acknowledge that this underestimates the regional population incidence which would be nearer to 35-40% if fractures treated locally out with the trauma centre were included. Seven hundred and two (86.1 %) were displaced proximal humeral fractures (fracture-complexity groups 2–4); 397 of 815 (48.7 %) were complex proximal humeral fractures, with three or more parts including fracture dislocations and head-splitting fractures (fracture-complexity groups 3 and 4). Of these 397 fractures, 226 (56.9 %) were women over 60 years, and 69 (17.4 %) were men under 60 years. According to the AO classification, 375 (46.0 %) had type A, 181 (22.2 %) type B and 259 (31.8 %) type C. According to AO classification, the three most common groups were A3 [210 (25.8 %)], C2 [193 (23.7 %)] and A1 [103 (12.6 %)]. The majority of complex fractures occurred in older women with fracture complexity groups 3 and 4 based on Neer and AO classifications 5.3 and 5.1 times more common, respectively, in women over 60 years than in men of the same age group.

A Japanese population based study categorised 509 fractures according to the Neer classification(66). There were 185 cases (36%) of one-part fractures, followed by 156 cases (31%) of 2-part surgical neck fracture, 60 cases (12%) of 2-part greater tuberosity fracture (dislocation included), 45 cases (8.8%) of 3-part fracture involving the greater tuberosity and the surgical neck (dislocation included), 31 cases (6.1%) of 4-part fracture (dislocation included), and 17 cases (3.3%) of valgus-impacted fracture. Eight fractures (1.6%) could not be classified. In keeping with these results, a French study which included 329 fractures found the overall number of minimally displaced proximal humeral fractures to be 42 %(33).

1.5.5 **Summary of the existing fracture classifications**

In summary the Neer classification, which is almost 50 years old, remains the most commonly used in clinical practice. It has the advantage of simplicity and a reliance on plain radiographs. However, it fails to take account more recently described pathoanatomy that may provide additional prognostic information and is of relevance to new surgical techniques. Some newer classifications described above include additional relevant fracture configurations but are cumbersome and complex to use or are of limited scope describing only some of the fracture types. These new classifications can be viewed as ‘descriptive modifiers’ of the original Neer classification which might inform treatment and outcome for some fracture subtypes. However, there is at present no comprehensive classification for use in the prediction of prognosis and choice of treatment. Only when an adequate classification system is available will surgeons be able to collaborate to produce well-designed comparative clinical outcome studies, to enable proper evidence-based management of these injuries.

1.6 NATURAL HISTORY

Stable, nondisplaced fractures have a high union rate and satisfactory functional outcome. Keser evaluated 27 patients with minimally displaced fractures and all were united at a mean of 25 months follow up(67). The mean Constant score was 81 and 23 patients (85%) had mild or no pain in the shoulder. Similarly all 104 patients with minimally displaced fractures in Koval's series united(68). Eighty patients (77%) had a good or excellent result, fourteen (13%) had a fair result, and ten (10%) had a poor result. Ninety- four patients (90%) had either no or mild pain in the shoulder. Functional recovery averaged 94%; forty-eight patients (46%) had 100% functional recovery. In a series evaluating range of motion in 67 patients with minimally displaced fractures, the range of shoulder motion of the affected side was diminished compared to the unaffected extremity in internal rotation and external rotation but not forward flexion(69). Patients largely returned to preoperative functional status at 1-year follow-up.

Displaced and complex multipart fractures have a less certain prognosis. Court Brown studied 131 displaced 2-part surgical neck fractures and found that nonoperative treatment yielded similar results to surgical treatment even with 66% or more displacement(70). In this series the choice between operative and conservative management was made by the treating surgeon, a potential source of selection bias. Outcome data evaluating the effect of surgery was only complete in 49 (37%) patients and only 18 (14%) underwent surgical treatment. Additionally, patients' subjective view of their progress was better than the objective measurement of range of movement and power would suggest. The results for flexion and abduction at one year were particularly poor and only 60% to 65% of power was regained by this time.

Court Brown also retrospectively assessed four-part valgus fractures in 125 elderly patients. This study reported a mean Constant score of 78.1 and a mean Neer score of 87.1 at one year follow-up, however the average power of shoulder flexion and abduction was only 75% of normal. These results might be over optimistic for more severe fracture patterns as a heterogenous group of fracture displacements were included in this study. 57 (46%) patients had minimally displaced fractures and only 31 (25%) patients had fractures with displacement of both the surgical neck and the greater tuberosity. In the presence of surgical neck and greater tuberosity displacement there was a decrease in shoulder function, related to loss of flexion and abduction power.

Other studies evaluating nonoperative treatment of displaced fractures have yielded poor outcome results(71). In a prospective cohort study, Torrens examined nonoperative treatment 70 patients with both displaced and non-displaced proximal humerus fractures(72). While healing occurred in most patients, Constant scores decreased with worsening severity of fracture. Functional outcomes improved progressively from four part to three part and subsequently two part fractures. Pain outcomes worsened with three and four part fractures in relation to two part injuries, The authors concluded that patients with more severe and displaced fractures should be counselled about the possibility of inferior outcome. Kristiansen randomized a group of two- three- and four-part fractures to either closed treatment or external fixation(73). Of the 11 fractures treated nonoperatively, nonunion occurred in 2 surgical neck fractures and 2 greater tuberosity fractures and 2 patients developed AVN of the humeral head after one year. The median Neer score was 60 with satisfactory results only achieved in 4 of 11 patients.

A more recent study investigated the relationship between displacement and outcome in nonoperatively treated proximal humerus fractures(51). Radiographs and CT scans were used to classify patterns of displacement into posteriormedial (varus) impaction, lateral (valgus) impaction, isolated greater tuberosity, and anteriomedial impaction. Head orientation, impaction of the surgical neck, and displacement of the tuberosity correlated with outcome in this series. As both posteriomedial and greater tuberosity displacement increased, outcome worsened. Overlap of the greater tuberosity with the posterior articular surface was associated with a worse outcome. In varus, or posteriomedial, impaction, outcome worsened as the articular surface displaced inferiorly and increased the distance from the acromion. Another study found that humeral head angulation on initial radiographs correlated with ultimate functional outcome(74). Angulation of the humeral head on both a standard AP projection and scapular lateral view had a significant association with Constant score.

In summary, very little high level evidence exists assessing the natural history of proximal humerus fractures(71, 75-77). Poor outcome following proximal humerus fracture is often mediated by development of a complication related to the injury. The three major complications encountered in clinical practice are nonunion, rotator cuff dysfunction and avascular necrosis. Whilst it is accepted that each of these complications are associated with a suboptimal outcome, at present there is no reliable means of predicting which patients are at highest risk. The following section reviews these three complications of proximal humerus fractures.

1.6.1 **Nonunion**

Nonunion of the head to the shaft after NHF is a debilitating complication, the prevalence of which is unclear, with reported rates ranging from around 1% to 20%(3, 78-80). The vast majority of nonunion studies focus on surgical treatment rather than population based epidemiology(81-84). The only study specifically investigating the epidemiology of nonunion reported an overall incidence of 1.1%, rising to 10% if there was translation of the surgical neck(1). This study may have underestimated the true incidence as 19% of the patients in this series had an isolated greater tuberosity fracture and therefore were not at risk a nonunion between the humeral head and shaft. Furthermore 112 (11%) patients, with presumably more severe fracture patterns underwent primary operative fixation.

Whilst there is no single, universally accepted, definition of fracture union, many studies define a fracture to have healed when a patient has no or minimal pain, no or minimal functional limitation, no mobility at the fracture site, and evidence of radiological union(85, 86). Radiological union following NHF has been defined as trabeculation across the fracture on both views or, in those fractures which were displaced, when the lateral bone bridge is complete(3).

In clinical practice the diagnosis of nonunion is characterised by loss of normal function and clear radiological abnormality. Pain, stiffness and loss of function are the most consistent complaints. On examination, the patient often has a 'pseudoparalysis' of the deltoid, rotator cuff and periscapular muscles. Attempted movement of the shoulder is painful and any motion occurs in the fracture site rather than the glenohumeral joint. Radiologically there is resorption and widening of the fracture line often with massive bone loss.

Nonunion following NHF is poorly tolerated in the majority of physiologically younger patients and it is often only possible to achieve sustained pain relief with operative treatment. This can be challenging due to capsular scarring, bone loss, distorted anatomy and osteopenia of the humeral head(87, 88).

There is evidence that fractures should be united by 3 months(3). Patients with nonunion have been shown to have poor outcome scores 3 months following injury, with very little improvement between 3 months and 6 months. If treatment is delayed, shoulder function deteriorates after 6 months. Furthermore, progressive disuse osteopenia and prolonged delay may compromise operative fixation. Nonunion should therefore be treated by 6 months at the latest, but due to the relatively small improvement between 3 and 6 months, it has been suggested that the diagnosis should be made and treatment initiated at the 3 month stage(3).

Although nonunion may occur for no apparent reason, there are usually patient or injury related characteristics which might have acted as predisposing factors and its cause in individual patients may be multifactorial. The effect of patient related factors on fracture healing is controversial. Age, sex, diabetes, use of medications such as corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), smoking, excessive alcohol use, and poor nutrition have been implicated however it is impractical to examine many of these factors in clinical trials and much of the evidence comes from case series with small sample sizes or from anecdotal reports. Furthermore, few authors report estimates of the magnitude of associations between potential risk factors and fracture-healing complications. Further work is warranted in this area(82, 89, 90). Whilst it would make sense that the fractures at most risk of nonunion are two-, three- or four-part fractures where there is minimal residual contact between the humeral head and shaft, this relationship is yet to be proven in clinical studies. Biomechanically, the complete disruption of the periosteal sleeve leads to instability and soft tissue interposition of periosteum, muscle, and the tendinous portion of the long head of biceps may also inhibit callus formation(87, 88, 91).

Although involvement of these factors in the development of nonunion is plausible there is a paucity of evidence regarding the role of patient or injury characteristics as predictors of nonunion. Further work in this area, through large prospective studies is required to allow early identification and perhaps targeted treatment in patients at high risk of nonunion.

One of the main aims of this thesis is to identify risk factors for the development of nonunion. The study investigating this is reported in CHAPTER 4. Nonunion is an important outcome for assessing the value of a classification because it is readily diagnosed clinically and radiologically, frequently results in a poor functional outcome, and patients at risk of this complication may benefit from early surgical intervention(92).

1.6.2 **Rotator cuff dysfunction**

Malunion of one or both tuberosities is common and may result in varying degrees of morbidity. Whist it might be well tolerated in elderly patients with limited functional expectations, in physiologically younger patients, the altered shoulder mechanics produced by the defunctioning and tearing of the rotator cuff tendons and impingement of the displaced tuberosity fragments often produces significant pain and functional compromise.

A symptomatic tuberosity malunion will typically give rise to shoulder pain, which is usually located over the anterior deltoid. The pain is usually aggravated by use of the arm and particularly by forward flexion and, abduction and internal rotation.

1.6.3 **Osteonecrosis**

Osteonecrosis of the humeral head occurs as a result of loss of perfusion of the articular surface and subchondral bone and results in articular collapse and fibrosis. Hertel investigated the radiological risk factors for osteonecrosis following NHF and his work is discussed in detail in section 1.5.3. As is the case for nonunion, most reports associating patient risk factors with osteonecrosis are observational studies and many are either anecdotal or have used case-control methods resulting in relationships of assumed risk factors to osteonecrosis whose causality is questionable(93). Osteonecrosis of the humeral head may or may not be symptomatic and the head may collapse completely, or there may be partial involvement only(50, 55, 94). The spectrum of presentation and the lack of precise radiological guidelines for its assessment make diagnosis difficult. For this reason, osteonecrosis was not an important concept of the fracture classification described in CHAPTER 5. There is no standardised protocol for the treatment of osteonecrosis after NHF with studies reporting the use of various treatment modalities such as pharmacologics, core decompression with small-diameter drilling, arthroscopic-assisted core decompression, and bone grafting(95-100). Prospective, randomized studies are needed to determine the efficacy of these joint-preserving procedures. Resurfacing techniques have a role in treating articular surface loss and shoulder arthroplasty is recommended for patients with end-stage disease(101, 102).

1.7 MANAGEMENT

The goal in the treatment of NHF is to promote complication-free healing to recreate a pain-free, mobile, stable and functional shoulder joint. As stated above, there is good evidence that in the majority of patients with a simple fracture configuration this is best achieved with nonoperative treatment(1, 4, 103). These patients will usually regain a level of shoulder function sufficient to meet their needs and the risk of complications are low.

The management of patients with more complex injury patterns remains controversial. There are several recent meta-analyses of the existing literature that have highlighted a paucity of level I, II or III evidence(71, 75-77). Most studies are retrospective case series. The characteristics of patient groups differ between studies because of inconsistencies in classification and patient selection. None of commonly used fracture classifications are robust enough to reliably facilitate comparison between different treatment methods. Most series are insufficiently powered to support any statistical conclusions and patients with different injuries are often combined to increase group size. General applicability may be uncertain as reports are often from a single surgeon reporting a single technique. Furthermore, the majority of data comes from centres of excellence, where the injury patterns encountered may be different from those encountered in everyday practice. The results reported by shoulder specialists, working in tertiary referral centres, may not be reproducible in centres where expertise or resources are more limited. Many operative series report on younger patients with more benign injury patterns, as a result of selection bias the same results may not be achieved in the elderly. Given the limitations of these studies, it is clear that contemporary, large scale, well-designed comparative clinical outcome studies are essential to enable proper evidence-based management of proximal humerus fractures.

The Proximal Fracture of the Humerus: Evaluation by Randomisation (PROFHER) study was the first randomised control trial that aimed to examine whether surgical treatment compared with nonoperative treatment results in better patient-reported outcomes for displaced fractures of the proximal humerus involving the surgical neck(104).

The investigators recruited 250 patients with a mean age of 66 who presented at the orthopaedic departments of 32 UK hospitals from September 2008 to April 2011. The patients were followed up for two years, and data from 114 patients in the surgical group and from 117 in the non-surgical group were included in the primary analysis. Patients allocated to surgery received either internal fracture fixation or arthroplasty. Those allocated to nonoperative treatment were given a sling for the injured arm followed by active rehabilitation.

The researchers found no statistically or clinically significant differences between surgical and non-surgical treatment as assessed using the Oxford Shoulder Score, which provides a total score based on the patient's subjective assessment of pain and function. The mean score over a two year period was 39.07 points in the surgical group and 38.32 points in the non-surgical group - a difference of 0.75 points (95% confidence interval –1.33 to 2.84; P=0.48). They also found no clinically or statistically significant differences between the two groups on measures of health related quality of life; complications related to surgery or shoulder fracture; complications needing secondary surgery or treatment; or death. The study found 10 medical complications (two cardiovascular events, two respiratory events, two gastrointestinal events, and four others), all of which occurred in the surgical group during the postoperative hospital stay. They concluded that 'these results do not support the trend of increased surgery for patients with displaced fractures of the proximal humerus'.

There are however significant concerns regarding the conclusion of the PROFHER study relating to the methodology of the trial. Due to the absence of an adequate classification system, it was not possible to include a homogenous subgroup of fractures based on defined radiological criteria. Rather, patients were recruited if they had 'a degree of displacement sufficient for the treating surgeon to consider surgical intervention'. As a result of this, out of 1250 patients assessed for eligibility, 1000 patients were excluded from the study for various reasons, amongst which was 'because there was a clear indication for surgery'. Therefore, only patients with an unclear indication for surgery were included in this study. After all exclusions had been made, there remained a selected group of 250 fractures for which, based on contemporary practice, indication for surgery was unclear. It could be argued that in practice, surgeons would generally choose conservative treatment if the indication was unclear. Rather than clarify the indications for surgery, this study appears to show that for a subgroup of patients in which the surgeon does not see a clear indication the expected outcome of various treatments is similar. A robust, reliable and standardised classification is required in order to answer the key question of which patients might benefit from surgery.

1.7.1 **Current treatment recommendations**

Due to the lack of good quality evidence on which to guide a decision regarding the best management for the minority of physiologically younger patients with complex proximal humerus fractures an individualised approach should be adopted taking into account patient and injury related factors.

Patient factors

Most patients with NHF are elderly and have limited expectations of treatment. Relative contraindications to operative treatment include the very elderly (aged > 85 years), cognitive impairment, a non-functional limb, or sever medial comorbidity. Intuitively, poor outcomes and increased complications might be expected in patients with severe osteoporosis, smoking, drug and alcohol abuse, diabetes mellitus, rheumatoid arthritis, immunocompromised including steroid medication and concurrent neoplasm however high level evidence to guide patient selection is lacking (70, 103, 105).

Fracture type

Currently available fracture classifications are of no proven value in the prediction of outcome or choice of treatment in patients with complex multi fragment fractures. The Neer classification, although widely used, does not include some of the more recently described fracture subtypes including impacted-valgus fractures, varus fractures and those with partial articular involvement due to a displaced tuberosity fragment bearing a piece of the articular surface. A more adequate fracture classification would permit better definition of specific fracture morphologies that might benefit from surgical fixation.

1.8 LIMITATIONS OF EVIDENCE AND DIRECTION OF RESEARCH

Previous epidemiological studies describe series of proximal humerus fractures which include isolated tuberosity fractures as well as NHF. However the pathoanatomy, natural history and treatment options for isolated tuberosity fracture is different from that of injuries where there is involvement of the neck of humerus (with or without tuberosity involvement). There is therefore a need to investigate the subgroup of proximal humerus fractures with NHF.

Many of these studies of proximal humerus fractures have been conducted in the tertiary care setting. There is a need for epidemiological data regarding NHF to be conducted in geographically defined populations.

An association between social deprivation and proximal humerus fracture has recently been reported. This association remains to be established specifically in NHF. These questions are addressed in the epidemiological study reported in CHAPTER 3.

There is a paucity of data regarding the determinants of outcome of NHF. Nonunion is a debilitating outcome that might be preventable if at risk patients were identified early and offered appropriate surgery. However, there is currently uncertainty about its prevalence and the factors which predispose to its development. Clarification of these issues will allow better risk stratification and facilitate decision making in treatment and patient counselling. The results of a study to develop and evaluate a risk prediction formula for NHF this is reported in CHAPTER 4 and CHAPTER 7.

The evaluation of surgical treatment of NHF is challenging and at present there is no high level evidence to support surgical intervention. This is probably due to weaknesses in previous studies which have included disparate patient groups and failed to identify patients at high risk of poor outcome as subjects. This in turn reflects the fact that existing classification systems are of no proven value in predicting outcome.

Thus there is an urgent need for a new classification system for NHF. This should, in addition to predicting prognosis, be comprehensive - providing a means of describing all of the commonly encountered, clinically relevant fracture patterns, be based on a standard, easily obtained radiographic series and have an acceptable level of inter- and intra- observer reliability. Only when an adequate classification system is available will surgeons be able to collaborate to produce well-designed comparative clinical outcome studies, to enable proper evidence-based management of these injuries. A novel classification for NHF is presented in CHAPTER 5 and evaluated in CHAPTER 6 and CHAPTER 7.

1.9 THESIS AIMS

The aims of this thesis are to:

1. Investigate the epidemiology of NHF in a well defined geographical area.
2. Identify the prevalence of nonunion after NHF.
3. Identify risk factors for nonunion after NHF.
4. Develop and evaluate a formula for the calculation of risk of nonunion in individual patients.
5. Develop and evaluate a novel classification for NHF.

CHAPTER 2
NECK OF HUMERUS FRACTURE DEFINITION, STUDY SETTING AND CASE ASCERTAINMENT

2.1 CHAPTER AIMS

The purpose of this chapter is to describe the method used to define a NHF in the series of investigations reported in this thesis. The method that was used to define the population at risk of NHF is described. The setting in which the studies took place and the methods of patient identification and data collection are described.

2.2 INTRODUCTION

The Edinburgh Orthopaedic Trauma Unit, based in Edinburgh Royal Infirmary, provides all orthopaedic trauma services to a well defined region of Scotland. with a stable population of over 500,000. This provides an important opportunity to study epidemiological aspects of NHF and investigate its natural history in patients presenting from a large, unselected, geographically based population. This thesis describes a series of studies in patients who have presented to the Edinburgh Orthopaedic Trauma Unit with NHF. The purpose of this chapter is provide essential background information about the study population, definition of NHF, case ascertainment, and methodology that is relevant to the studies in all subsequent chapters. It will be used to describe:

1. Criteria adopted in this thesis for the diagnosis of NHF.

2. Method of assessment of radiographs when applying these criteria.

3. Setting in which the series of studies reported in this thesis was conducted.

4. Method of case ascertainment.

2.3 RADIOGRAPHIC ASSESSMENT AND DIAGNOSIS OF NECK OF HUMERUS FRACTURE

A proximal humerus fracture can be diagnosed using standard anteroposterior and modified axial radiographs however there are no standard radiological landmarks that separate the proximal humerus metaphysis and diaphysis. In the series of investigations that make up this thesis, a proximal humerus fracture was defined using a modification of the method of ‘squares’ as proposed by Urs Heim(45).

The traditional system of ‘squares’ is as follows: The proximal and distal segments of long bones are defined by a square whose sides are the same length as the widest part of the epiphysis in question. The diaphyseal segments are contained between the proximal and distal segments. In reality, many fractures that clinicians would consider to be of the proximal humerus extend outwith the proximal square and therefore the method of ‘squares’ was modified as described below.

A proximal square was drawn on the anteroposterior radiograph using the technique described by Urs Heim. A second square of identical proportions was then superimposed overlapping the distal half of the original square to produce a rectangle whose height was 50% greater than its width. This was defined as the proximal segment of the humerus (Figure 2-1).

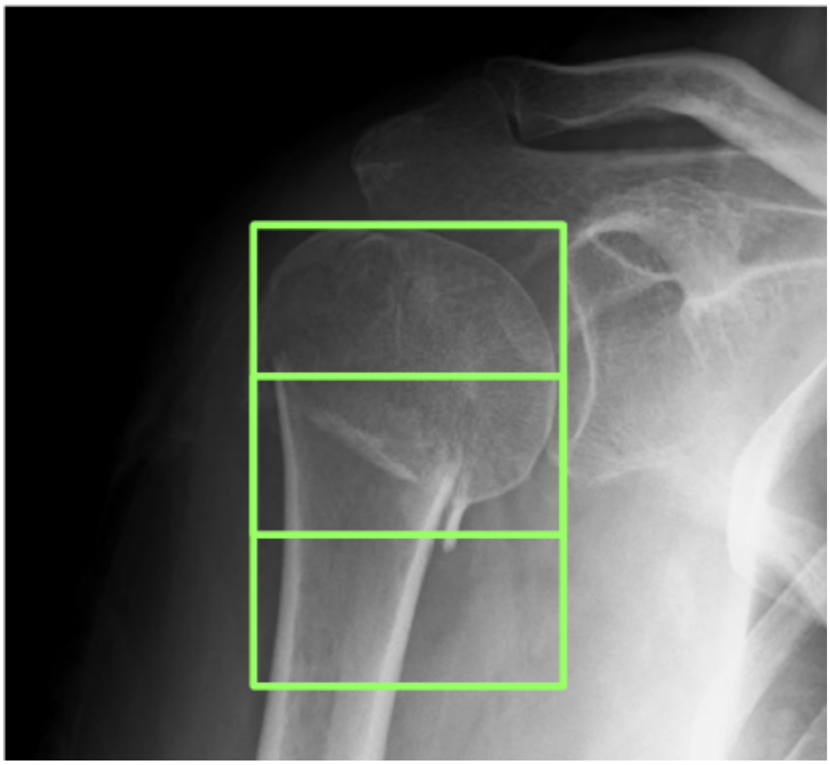


Figure 2-1 Modified method of 'squares' technique used to define the proximal segment of the humerus for the series of investigations reported in this thesis.

Before a fracture could be assigned to the proximal segment of the humerus, its centre had to be determined. In a simple fracture, it was possible to define the centre of the fracture without difficulty. In a wedge fracture, the centre was at the broadest part of the wedge. In a complex fracture, the centre lay halfway between the two principal fragments.

Any fracture confined to the proximal segment was defined a proximal humerus fracture. Any diaphyseal fracture with a displaced component involving the proximal segment was also defined as a proximal humerus fracture. If a fracture was only associated with an undisplaced fissure which reached the proximal segment it was defined as a proximal or diaphyseal fracture depending on its centre. Any fracture completely outwith the proximal segment was defined as a diaphyseal or distal humerus fracture. If the humerus had two completely separate fractures, one of which was in the proximal segment and one in the diaphysis or distal segment each fracture was considered separately.

Proximal humerus fractures can be subdivided into those that involve the neck of humerus and those that do not. Only fractures involving the neck of humerus were included in the series of investigations in this thesis. A NHF was defined as a fracture line beaching all four cortices of the proximal segment of the humeral shaft on standard anteroposterior and modified axial radiographs. Proximal humerus fractures that did not involve the neck of humerus and were therefore excluded included isolated greater and lesser tuberosity fractures and articular surface impression fractures. Commonly encountered fracture configurations either involving, or not involving, the neck of humerus are listed in Table 2-1 and Table 2-2.

Fractures involving the humeral neck (included in this thesis)
Isolated NHF
NHF with associated fracture of either or both tuberoisties
NHF with associated glenohumeral dislocation with or without an associated fracture of either or both tuberosities
NHF with extension into the humeral diaphysis
Segmental fracture involving the neck of humerus and the humeral diaphysis

Table 2-1 Fractures involving the neck of humerus.

Fractures not involving the humeral neck (excluded from this thesis)
Isolated fracture of either or both tuberosities without associated NHF
Fracture of either or both tuberosities with associated glenohumeral dislocation but without associated NHF
Glenohumeral dislocation with articular impression fracture but without associated NHF
Isolated humeral diaphyseal fracture without NHF

Table 2-2 Fractures not involving the neck of humerus.

2.4 STUDY SETTING

2.4.1 The Edinburgh Orthopaedic Trauma Unit

The series of investigations in this thesis all took place at The Edinburgh Orthopaedic Trauma Unit. Edinburgh Royal Infirmary is the only orthopaedic trauma unit treating adults in the City of Edinburgh, Midlothian and East Lothian. All orthopaedic trauma patients in the area attend the hospital, and all outpatient fractures are reviewed at outpatient clinics. The orthopaedic trauma unit is a tertiary referral centre for orthopaedic trauma, receiving fracture referrals from the ED, local general practitioners, local minor injury units, as well as occasional referrals from other centres. The orthopaedic trauma unit is ideally placed to identify acute fractures that present to the health care services in Edinburgh.

2.4.2 Neck of humerus fracture treatment protocol

Initial assessment and treatment

During the study periods, the initial assessment and treatment of patients presenting with NHF was in the Accident and Emergency Department. All patients underwent standard anteroposterior and modified axial radiographs of the injured shoulder. Following diagnosis of a NHF, the injured shoulder was immobilised in a collar and cuff and the patient wass given oral analgesia. The majority of patients were discharged home from the Accident and Emergency Department on the day of injury. The remainder of patients were admitted from the Accident and Emergency Department to an inpatient orthopaedic ward.

Primary treatment decision

Patients who were discharged home from the Accident and Emergency Department were reviewed by an orthopaedic trauma consultant at the fracture clinic within the following week. Patients who required hospital admission were reviewed the following day by an orthopaedic trauma consultant. The definitive decision to offer primary nonoperative or operative treatment was made at this stage on an individual basis by the treating surgeon. There was no fixed protocol for offering surgical intervention, however the treatment decision was influenced by patient factors in addition to the fracture configuration. The fracture patterns described in Table 2-3 were considered for operative intervention in physiologically young and active patients who were medically fit for surgery. Patients undergoing primary operative treatment underwent surgery within 2 weeks of their injury.

Fracture patterns considered for operative intervention
Unstable two-part surgical neck fractures in which there was disengagement of the shaft from the humeral head, due to displacement or extensive metaphyseal comminution.
Two-part greater or lesser tuberosity fractures, or three- and/or four-part fractures in which the greater tuberosity was displaced by more than 1 cm.
Fractures with a displaced fragment of the articular surface of the humeral head attached to a displaced tuberosity fragment.
Two-, three- or four-part fractures in which there was varus or valgus deformity of the humeral head to the shaft by > 30° from the normal head shaft inclination angle of 130°.
Three- or four-part anterior fracture-dislocations caused by propagation of a posterior humeral head fracture (‘Hill-Sachs lesion’) and with retained soft-tissue attachments to the humeral head at surgery.
Three- or four-part posterior fracture-dislocations caused by propagation of a fracture of the anterior humeral head (‘reverse Hill-Sachs’) and with retained soft-tissue attachments to the humeral head at surgery.

Table 2-3 Fracture patterns considered for operative intervention.

Nonoperative treatment

Patients treated nonoperatively had the shoulder immobilised for three weeks in a collar and cuff. They were reviewed in the fracture clinic three weeks following injury and underwent standard anteroposterior and modified axial radiographs of the injured shoulder. The collar and cuff was discarded at this time and patients began gentle, pendular shoulder exercises. Further clinical and radiological review was undertaken six weeks following injury. Progressive shoulder range of movement and strengthening exercises began at this time under the supervision of a physiotherapist.

Clinical follow-up

Fracture union was assessed by clinical examination and standard anteroposterior and modified axial radiographs. A fracture was judged to be united when a patient has no or minimal pain, no or minimal functional limitation, no mobility at the fracture site, and trabeculation across the fracture on both views or, in those fractures which were displaced, when the lateral bone bridge was complete. Patients were discharged from follow-up when their fracture had united. Nonunion was judged to be present if there was absence of radiological union and any of ongoing pain, functional limitation or mobility at the fracture site three months following injury. Patients with nonunion who were physiologically young and active and were medically fit for surgery were offered secondary operative treatment at this stage.

2.5 CASE ASCERTAINMENT AND DATA COLLECTION

Two separate databases were collected and analysed for the series of investigations reported in this thesis. The methods of data collection for each database are detailed in this section.

2.5.1 **Case ascertainment protocol**

Database 1 details the group of patients investigated in the studies reported in CHAPTER 3 and CHAPTER 4. Database 2 details the group of patients investigated in the studies reported in CHAPTER 6 and CHAPTER 7.

Database 1: January 2002 to December 2008

All inpatients and outpatients presenting to the Orthopaedic Trauma Unit of Edinburgh Royal Infirmary with an acute fracture of the neck of humerus were prospectively recorded for a seven year period between 1st January 2002 and 31st December 2008.

Throughout the seven year study period fracture information was prospectively gathered by audit workers either following the initial fracture clinic appointment or admission to the orthopaedic ward. A NHF diagnosis was made by examining each set of radiographs and applying the diagnostic criteria as described in section 2.3. In cases where the diagnosis was not clear from initial radiographs, further information was obtained from the accompanying radiology report, the referring clinicians' examination findings, the orthopaedic clinicians' examination findings, and the results of further imaging.

Database 2: November 2013 to October 2014

All inpatients and outpatients presenting to the orthopaedic trauma unit of Edinburgh Royal Infirmary with an acute fracture of the neck of humerus were prospectively recorded for a one year period between 1st November 2013 and 31st December 2014.

Throughout the one year study period fracture information was prospectively entered into an electronic database. Every patient had their radiographs reviewed by an orthopaedic trauma consultant and a diagnostic code was assigned. In cases where the diagnosis was not clear from initial radiographs, further information was obtained from the accompanying radiology report, the referring clinicians' examination findings, the orthopaedic clinicians' examination findings, and the results of further imaging. The author (EBG) reviewed the radiographs for each fracture to confirm the diagnosis using the criteria described in section2.3.

2.5.2 **Inclusion and exclusion criteria**

Patients with a NHF as defined in section 2.3 were included. Patients who had a proximal humerus fracture that did not involve the neck of humerus were excluded.

Adult patients residing in the City of Edinburgh, Midlothian and East Lothian were included. Patients residing outwith this catchment area (as determined by address and postal code) were excluded, but Edinburgh residents injured elsewhere and followed up at the orthopaedic trauma unit were included. Orthopaedic care for West Lothian residents is shared with a second institution, and therefore all West Lothian residents were excluded.

Children in Edinburgh are treated at a separate paediatric hospital. The threshold for transfer to the adult hospital is 13 years of age, but a number or 13, 14 and 15 year olds are known to be treated at the paediatric hospital. This study was therefore limited to patients aged 16 years or older.

Only patients surviving long enough to be referred from the ED for orthopaedic treatment were included. Patients noted to be 'deceased on arrival' at the RIE, or who died in the ED, were excluded. Fragility fractures and other pathological fractures were included but acute periprosthetic fractures were excluded.

2.5.3 **Multiplicity**

For the purpose of data analysis and statistical testing, multiple events were treated according to the following criteria, which are in keeping with previously published fracture epidemiology work(2):

1. A single fracture occurring in any adult patient was recorded as 'one fracture, one patient'.
2. Recurrent NHF episodes in the same patient over time were recorded as 'two fractures, one patient', with any subsequent recurrences added accordingly.
3. Bilateral NHF occurring at the same time were considered as separate fractures.
4. Segmental NHF with involvement of the humeral diaphysis of the distal humerus were counted as one NHF.

2.5.4 **Data collection**

The following data were prospectively recorded by audit workers for database 1 and by the author (EBG) for database 2.

Demographic data

Demographic information included date of birth, date of injury, age, gender, address and postal code.

Deprivation data

Each patient's postal code was recorded in order to allow deprivation data to be obtained from Scottish Government sources. The Scottish Index of Multiple Deprivation (SIMD) combines 38 indicators of deprivation across seven broad domains: income; employment; health; education, skills and training; housing; geographic access to services; and crime. Each of these deprivation domains is weighted on relative importance (28%; 28%; 14%; 14%; 9%; 5%; 2%) to give the overall deprivation index. The SIMD identifies small area concentrations of deprivation based on postal code groupings known as datazones. Scotland contains 6,505 datazones, and these are ranked from the most deprived (rank = 1) to the least deprived (rank = 6,505) areas. The rankings are often displayed as five or ten equal population categories (known as quintiles or deciles). The SIMD provides a *relative,* and not *absolute,* measure of deprivation. It is incorrect to assume that the datazone ranked 50 is twice as deprived as the datazone ranked 100. For the purpose of this study, each postal code in the City of Edinburgh, Midlothian and East Lothian was assigned a SIMD ranking.

Causation data

The circumstances surrounding the occurrence of acute NHF were recorded, and an attempt was made to categorise these as the *mode* of injury. The term *mechanism* was deliberately avoided, as it is seldom possible to determine the precise mechanism by which a fracture is sustained (*e.g.* torsional stess, axial loading *etc*). The criteria listed in Table 2-4 were adhered to.

Mode of injury	Criteria
Simple fall	Caused by a fall from a standing height, including twisting injuries.
Fall down stairs	Caused by a fall down stairs including twisting injuries.
Fall from a height	Caused by a fall from a height of six feet or more, excluding falls down multiple stairs.
Sporting injury	Injury sustained during sport participation or other athletic injury.
Road traffic injury	Injury to a vehicle occupant, pedestrian, cyclist, motorcyclist resulting from an accident on a road.
Other	Encompassing all other injury modes, including cases where the mode was unknown due to amnesia of events, alcohol intoxication or cognitive impairment.

Table 2-4 The criteria used to determine and classify the mode of injury responsible for acute fractures in the population served by Edinburgh Royal Infirmary.

Additional demographic data collection in database 2

In database 2 smoking status, alcohol intake, medical comorbidities and level of independence were recorded in addition to all of the above information. This data was obtained from review of the electronic patient records. For smoking status, patients were either classified as current smokers or non smokers. The number of cigarettes smoked per day was not recorded. For alcohol intake patients with a documented history of excess intake were recorded as such. Those without a documented history were recorded as not excess drinkers. This quantity of alcohol intake for each individual patient was not recorded. Patients with the following medical comorbidities were recorded as such if the medical comorbidity was documented in the electronic patient record: cardiac disease, respiratory disease, renal disease, liver disease, active malignancy, diabetes, hypertension, stroke, inflammatory joint disease and mental illness. Patients were either recorded as living independently or as having formalised care assistance of any type.

2.6 BACKGROUND POPULATION AND FRACTURE INCIDENCE

Fracture incidence was calculated using population data for the City of Edinburgh, Midlothian and East Lothian council areas obtained from the General Register Office for Scotland (GROS). UK census was carried out in 2001 and 2011, and the GROS annually calculated mid-year population estimates for each council based upon these data for each year of the study period. The starting point for mid-year estimates is the resident population on 30th June in the previous year. Data on births, deaths and migration trends for the preceding 12 months are taken into account. A full and detailed account of the methodology used by GROS to produce the annual mid-year population estimates is available on the GROS website. Deprivation data for the population at risk were obtained from Scottish Government sources, allowing the calculation of fracture incidence in relation to the SIMD.

CHAPTER 3
EPIDEMIOLOGY OF NECK OF HUMERUS FRACTURES

3.1 CHAPTER AIMS

The aim of this chapter was to investigate the epidemiological characteristics of NHF in a well defined geographical area.

3.2 INTRODUCTION

In the absence of any studies with a specific focus on the group of patients with NHF our understanding of the epidemiology of this fracture relies on the proximal humerus fracture literature. Much of this has been reported from tertiary care centres where referral patterns and case selection may have influenced results. This has been reviewed in CHAPTER 1.

NHF accounts for 80% of proximal humerus fractures, which with an annual incidence of between 63 and 105 per 100,000, account for 5% of all fractures of the appendicular skeleton(1, 2, 21).

Proximal humerus fractures predominantly occur in women and incidence rises progressively with age(1, 36, 64). Men present at a younger age than women. An increase in annual incidence has been reported(33, 64).

The vast majority result from low energy falls. However those associated with high energy injuries occur in a younger age group. This implies an important aetiological role for osteoporosis.

There is increasing awareness regarding the relationship of fracture epidemiology and socioeconomic deprivation in proximal humerus fractures however this has not been described specifically in NHF(37, 106, 107).

The natural history and management of NHF differs from that of isolated tuberosity fracture and there is thus a need for epidemiological investigation focusing specifically on NHF in a setting where the effects of referral pattern and case selection are minimised. The study described in this chapter provides the first account of the epidemiological characteristics specifically of a NHF population as well as demographic context for the study reported in CHAPTER 4.

3.3 MATERIALS AND METHODS

3.3.1 **Data collection**

Database 1 was used to investigate epidemiological aspects of NHF sustained between 1st January 2002 and 31st December 2008. The study setting, method of case ascertainment, inclusion criteria and demographic data collected is described in detail in CHAPTER 2.

All of the patients included in this study had a NHF. Patients with a proximal humerus fracture that did not involve the neck of humerus were excluded. Demographic data collected included patient age, gender, mode of injury and deprivation quintile.

3.3.2 **Statistical analysis**

Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington) and SPSS version 21.0 (SPSS, Chicago, Illinois) were used to undertake statistical analysis. Data were checked for normality using the Kolomogorov-Smirnov test. Continuous data were presented in terms of the median, range and interquartile range if asymmetrically distributed, and the mean and standard deviation if symmetrically distributed.

The Mann-Whitney U test was used to compare nonparametric continuous data between a dichotomous variable and the Kruskall-Wallis test was used to compare nonparametric continuous data when a variable had more than 2 categories. Groups of categorical variables were compared using the Chi square test.

Fracture incidence was calculated as the number of fractures per 100,000 of population per year (n/100,000/yr). The 95% confidence interval around the rates was estimated using the cumulative Poisson distribution which is a statistical distribution that shows how many times an event is likely to occur within a specified period of time.

Trends in fracture epidemiology were described according to the study year, age at the time of fracture, sex, mode of injury and deprivation. Age- and sex-specific facture distribution curve were produced. Fracture distribution curves were originally set out by Court-Brown and Caesar(31). They determined that there were 8 fracture distribution curves that accounted for the female and male incidence of all fractures, and their use is now recognized within fracture epidemiology(2). The curves are a measure of the changing incidence (y axis) with age (x axis). All curves are associated with peaks in incidence, such as unimodal or bimodal.

The Spearman correlation was used to determine the relationship between incidence and deprivation quintile. The "observed proportion" of fractures in each deprivation quintile was calculated by dividing the number of fractures in that quintile by the total number of fractures. The proportion of the population in that quintile was similarly derived. This served as the "expected proportion" in that the null hypothesis was that there was no difference in the proportion of fractures in each quintile. The observed proportion was, therefore, subtracted from the expected proportion to determine the absolute difference in proportion. This is a basic description of the associated chi-square statistic. For all of the epidemiological analyses, a two-tailed p value of <0.05 was considered statistically significant.

3.4 RESULTS

3.4.1 Population at risk

According to Scottish government sources, the population served by Edinburgh Royal Infirmary increased steadily from 511,848 in 2002 to 543,796 in 2008 (Figure 3-1). The number of females increased from 270,281 in 2002 to 285,89 in 2008 and the number of males increased from 241,567 in 2002 to 258,507 in 2008.

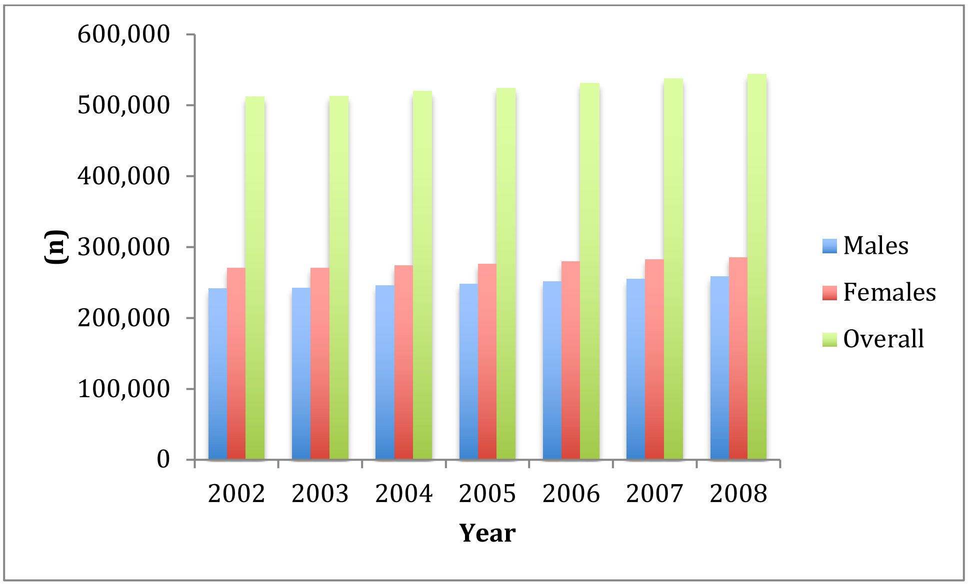


Figure 3-1 The population of adults, aged 16 years or older served by Edinburgh Royal Infirmary during each year of the study.

During each year of the study, females outnumbered males in all but the very youngest age category. The age- and gender related distribution of the population followed a similar trend throughout the study and this is shown diagrammatically for 2005 in Figure 3-2.

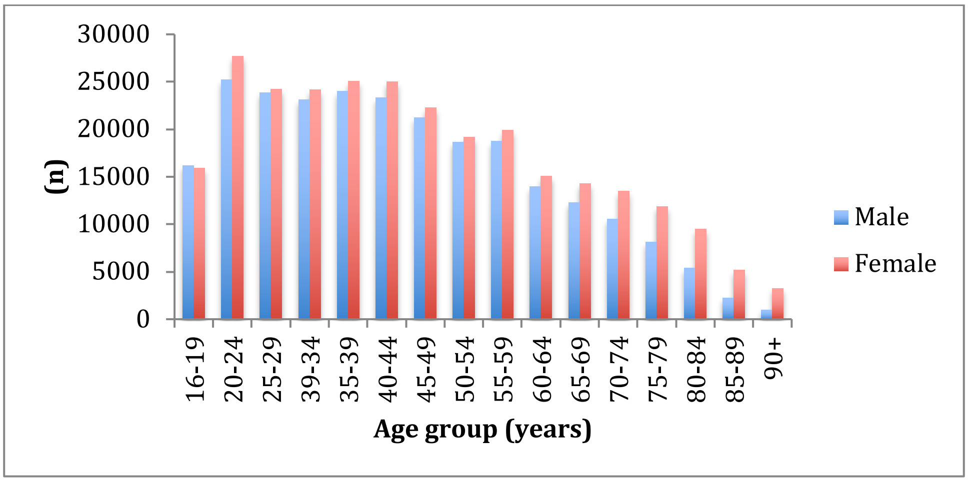


Figure 3-2 The age- and gender-related distribution of adults, aged 16 years or older, served by Edinburgh Royal Infirmary. Data were obtained from the General Register Office for Scotland and represent a mid-year population estimate for 2005 (n=524,266).

There was an uneven distribution of the population served by Edinburgh Royal Infirmary according to deprivation quintile. The overall population at risk was greatest in the most affluent quintile and smallest in the most deprived quintile (Figure 3-3).

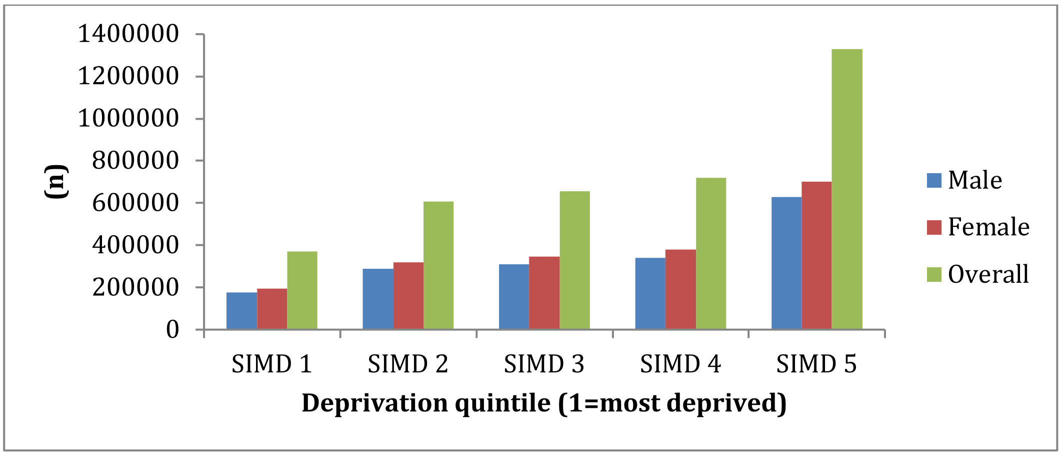


Figure 3-3 Overall number of patients at risk in each deprivation quintile throughout the whole study period.

3.4.2 Overall fracture incidence

In the seven-year study period, 2,683 factures were sustained by 2,632 patients. Nine patients had bilateral simultaneous fractures and a further 42 patients had two separate fractures. The overall incidence of NHF was 72.9 per 100,000 per year. Over the study period, the incidence remained stable between 2002 and 2007 but was higher in 2008 (84.0 per 100,000 per year) (Figure 3-4).

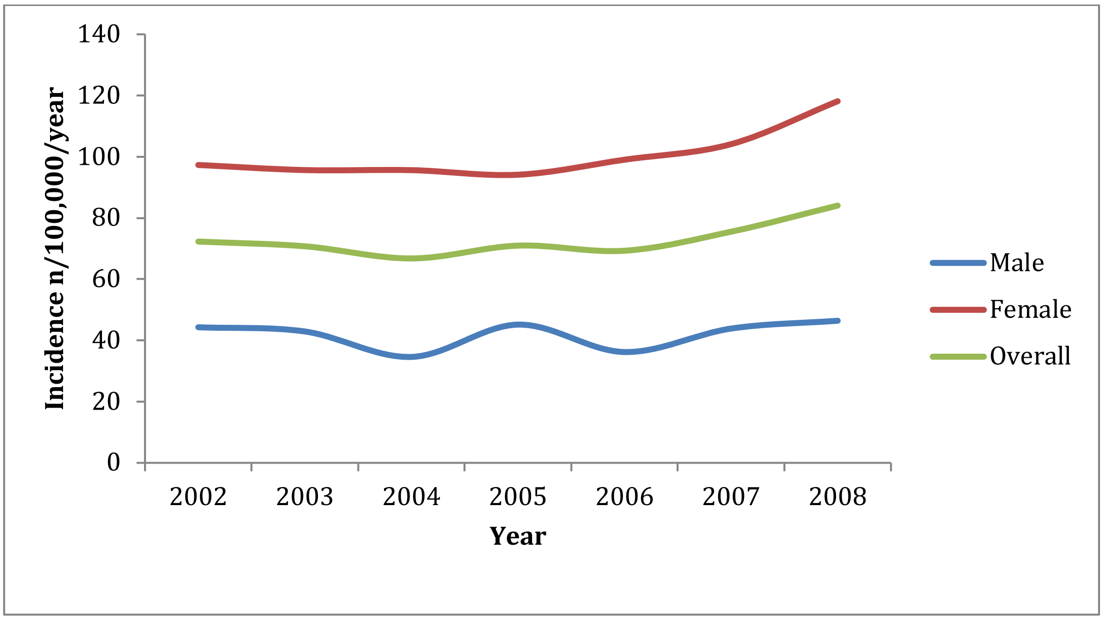


Figure 3-4 Incidence of NHF in each year of the study.

3.4.3 Sex and age distribution

Females sustained 1,952 fractures (72.8 percent) and males 731 fractures (27.2 percent). The overall gender specific incidences were 100.7 and 41.9 per 100,000 per year for females and males respectively (Figure 3-4).

The median age of all patients was 72 years (IQr, 58 – 81) with a range from 16 years to 103 years. The median age of females was 75 years (IQr, 64 – 82 yrs). They represented significantly older group than males, who had a median age of 62 years (IQr, 49 – 76 yrs), ($p < 0.001$, MWU test).

The fracture distribution curve shows a type F older male and female curve as proposed by Court-Brown and Caesar in 2006 (Figure 3-5)(2). The incidence in females dramatically increased every decade from the age of 40 years, peaking at 583.9 per 100,000 per year in the tenth decade. A steep increase was also seen in males but not until the age of 70 years, peaking at 213.8 per 100,000 per year in the tenth decade.

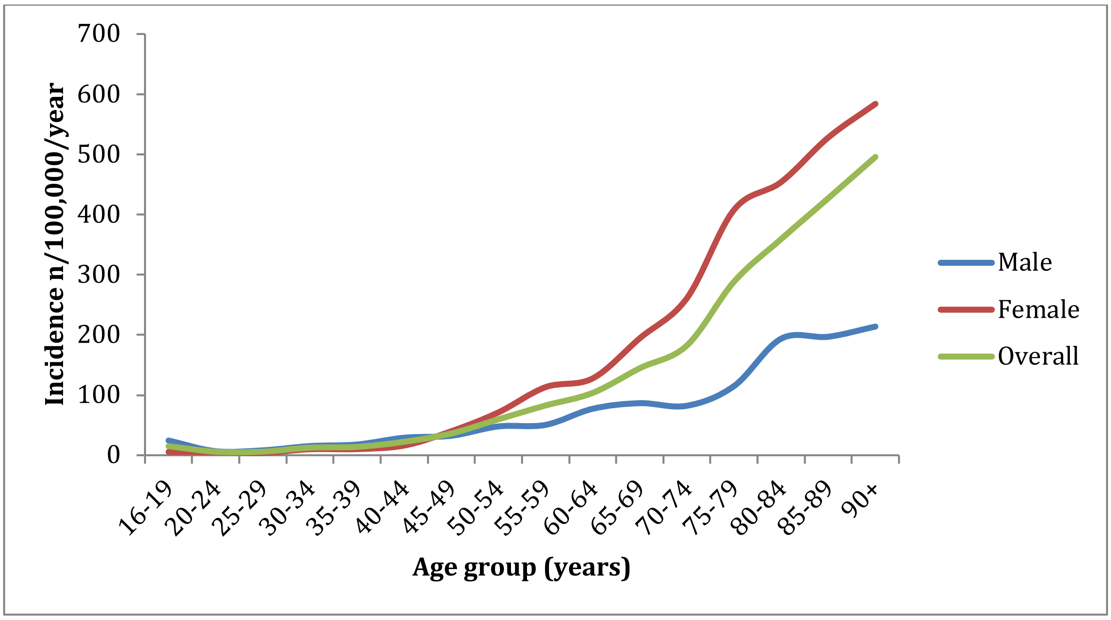


Figure 3-5 The age- gender-related incidence of NHF occurring in adults served by Edinburgh Royal Infirmary.

3.4.4 Mode of injury

Overall, the vast majority of factures (87.8 percent) were caused by a simple fall (Figure 3-6). The proportion of females sustaining their injuries in this way was greater; 91.9 percent of females as opposed to 76.9 percent of males ($p < 0.001$, Chi-square test). The remaining 12.2 percent of fractures were caused by higher energy injuries. These higher energy injuries occurred more frequently in males; although males accounted for only 27.2 percent of fractures, 51.5 percent of high energy injuries occurred in males. The sex difference in these higher energy fractures was most marked in fractures related to sport.

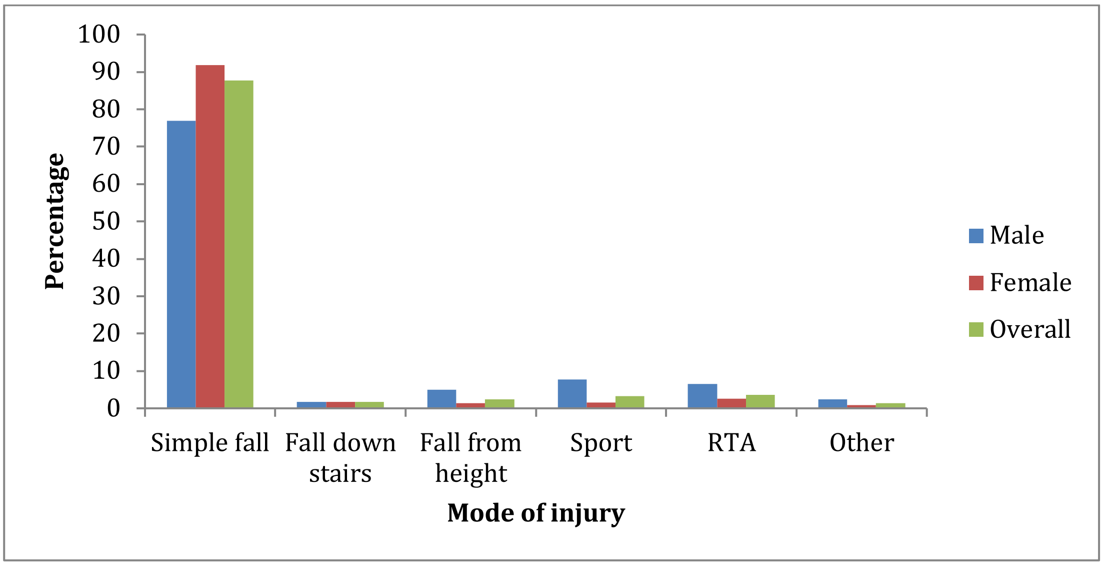


Figure 3-6 Percentage of NHF according to mode of injury and gender.

The mean ages for the different modes of injury are shown in Figure 3-7. Patients sustaining their injury through a simple fall were significantly older than those who's fracture was caused by a higher energy injury ($p < 0.001$, MWU test). In patients aged 16 to 34 years the most common modes of injury were sporting injuries and simple falls. In all groups aged more than 34 years of age, simple falls were responsible for the vast majority of injuries (Figure 3-8).

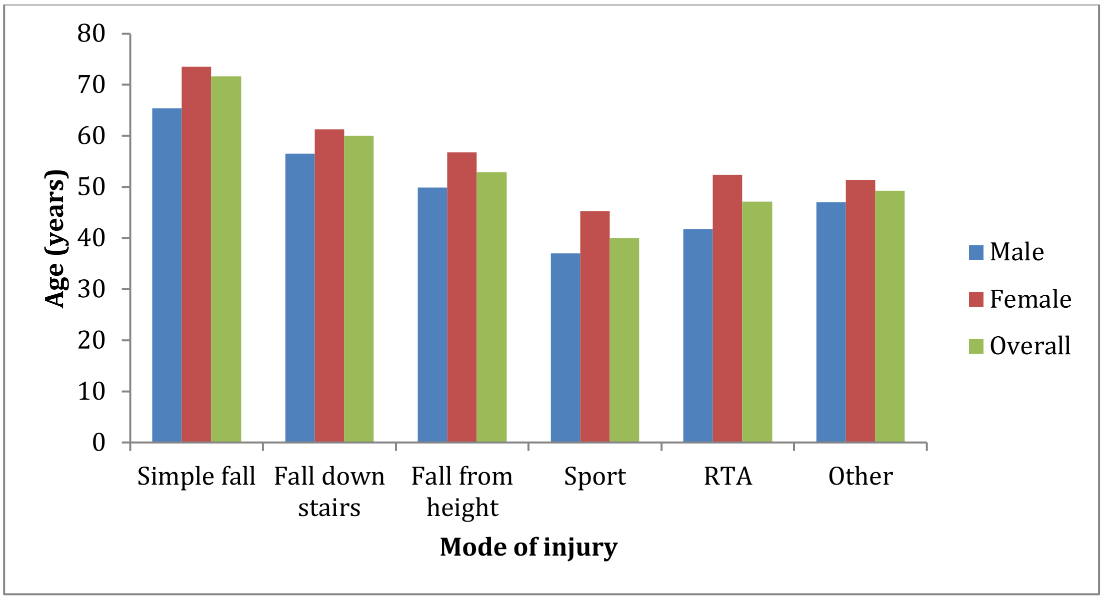


Figure 3-7 Patient age according to mode of injury and gender.

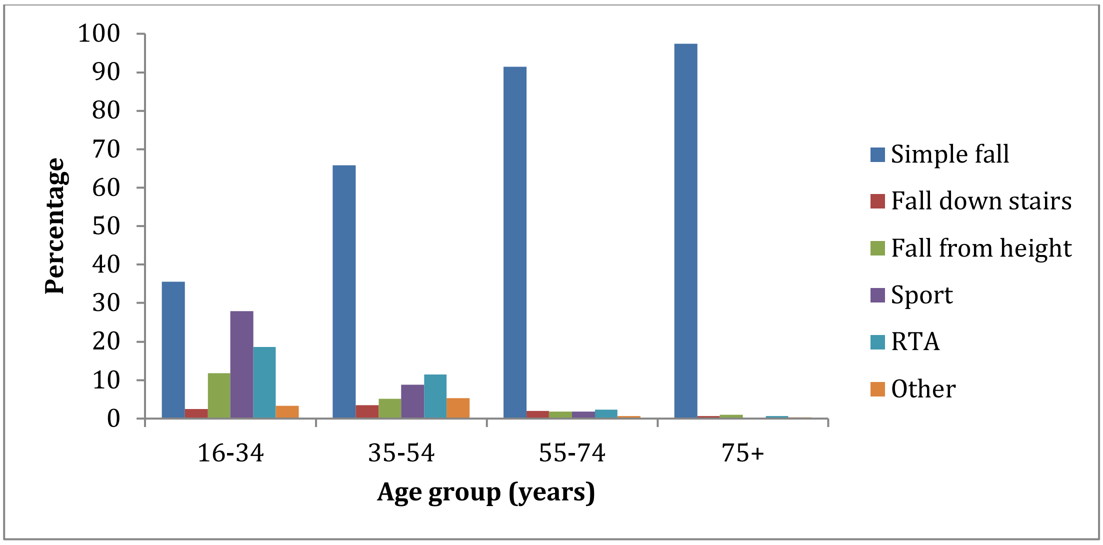


Figure 3-8 The distribution of injury modes causing fractures of the neck of the humerus arranged according to patient age group.

3.4.5 Deprivation

There was an unequal distribution of fractures according to deprivation (Figure 3-9), with a statistical trend towards an increasing incidence with increasing deprivation (*p* = 0.037, Spearman correlation coefficient, -0.900). In the most deprived category, the difference between observed and expected proportions was 0.3% more than expected and in the least deprived group it was 4.2% less than expected (Figure 3-10).

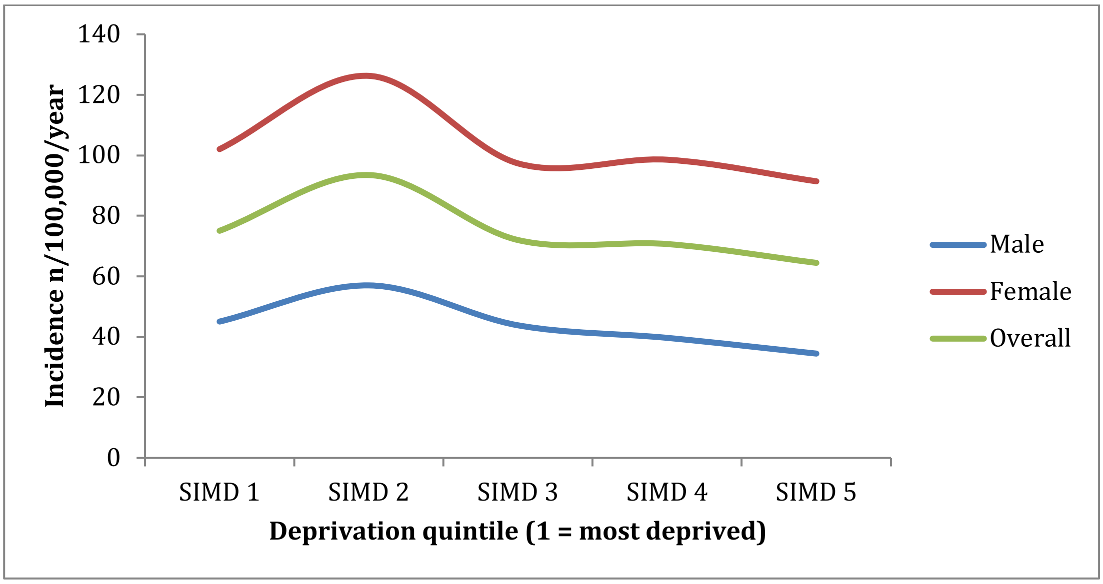


Figure 3-9 The association between NHF incidence and deprivation quintile.

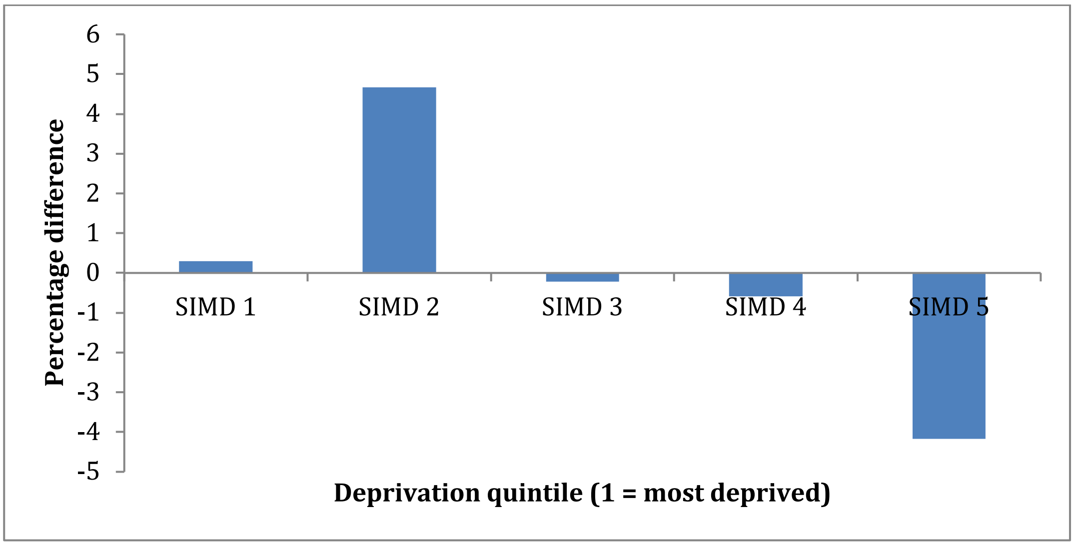


Figure 3-10 Percentage difference between observed and expected proportions of fractures by deprivation quintile.

Age varied significantly between the deprivation categories, with the least deprived patients sustaining their fracture at an older age ($p<0.001$, Kruskall-Wallis test). There was no association between deprivation quintile and gender ($p = 0.516$, Chi-square test) or mechanism of injury ($p = 0.424$, Chi-square test).

3.5 CHAPTER DISCUSSION

Fractures of the neck of humerus are common and the overall incidence over the study period was 72.9 per 100,000 per year, occurring primarily in the older female. This study concurred with others in finding a female to male ratio of 2.7:1(1, 37, 108). NHF appear to be predominantly fragility fractures as they follow a type F fracture distribution curve with an increase in incidence after the fifth decade in females and after the eighth decade in males.

The annual fracture incidence remained stable between 2002 and 2007 but increased to 84.0 per 100,000 per year in 2008. The age distribution of patients remained constant, so this was not responsible for the change seen in 2008. It is possible that the increased incidence in 2008 could be simply be within the limits of normal annual variation however there are other age adjusted studies reporting that proximal humerus fractures are becoming more common(109). The reason for this is not known but the usual explanations for osteoporotic fractures are decreased bone mineral density and the increased propensity for elderly people to fall (impaired balance, coordination, reaction time, muscle strength). It therefore may be the case that elderly people are less healthy and functionally capable today than in the past.

Earlier studies examining the epidemiology of proximal humerus fractures documented an average age of around 65 years(1, 37, 108). The median age at the time of fracture in the present study was 72 years with females significantly older than males. One reason for this discrepancy is that the background population of Edinburgh is relatively affluent with a high proportion of the population in SIMD5 and due to behavioural differences and better bone health, these patients may be more likely to sustain their fractures at a more advanced age. Another explanation for the older median age in the present study is that isolated tuberosity fractures were excluded and these tend to occur in younger patients(1, 37, 108).

This study has shown that almost 90% of NHF are caused by a fall from standing height. Fracture from these falls occurred even more frequently in females. Thus the typical NHF patient was not just older and female, but also sustained their fracture through a low energy injury. These findings are in keeping with the literature(1, 37, 108). In patients aged 34 years and younger, higher energy injuries were more common with almost 30% occurring during sport. The type F fracture distribution curve and predominance of low energy injuries suggests that NHF are fragility fractures, associated with osteoporosis.

Worsening social deprivation was associated with a statistically significant increased incidence of NHF. This has not previously been reported in NHF but is in keeping with other papers looking at the effect of social deprivation on other fractures(37, 106, 110-112). One explanation for the increased incidence with worsening social deprivation is behavioural difference, with younger socially-deprived patients sustaining their fractures during sporting activities and assaults, which has been demonstrated for other fractures(111, 113). A further explanation for this finding is that the least deprived patients have a better bone quality at a comparable age and therefore have fewer fractures at a younger age. Factors associated with socioeconomic status that may influence fracture incidence are physical inactivity, nutrition, alcohol, smoking and education(114, 115).

The SIMD does not publish the mean age for each for each data zone, so it is not possible to calculate the mean age of the population at risk in each deprivation quintile. NHF occurs predominantly in older patients and the incidence of fracture in each quintile is therefore likely to be influenced by the mean age of the background population in it. Despite this, the true age adjusted incidence is still likely to be higher in the most deprived quintile as the mean age of the background population is likely to be younger than that of the most affluent quintile.

The main strength of this chapter is that it represents prospectively collected data on a large series of patients over a 7 year period in a well demarcated population. The Edinburgh Orthopaedic Trauma Unit is the only centre providing a musculoskeletal trauma service for the local catchment area and it was therefore possible to accurately define the incidence of these injuries. This is the first series to specifically look at NHF, which have distinct epidemiological fractures from isolated tuberosity fractures. It is likely that if the isolated tuberosity fractures had been removed from Court-Brown' epidemiology study the NHF epidemiology in his series would be similar to that reported in the present study(1).

A weakness of this study is the lack of more detailed demographic data including pre injury level of function, smoking status, alcohol consumption and medical comorbidities which may influence fracture incidence. Additionally, this study used a methodology of categorising deprivation that has been used in many orthopaedic trauma studies from multiple countries(110, 115, 116). Yet it may be difficult to generalise the results because there is no collectively agreed standard for measuring socioeconomic status. However, the IMD is a universally applicable tool given that the factors used to determine deprivation are attributable to any developed population.

When performing epidemiological studies, there is debate about the reporting of multiple events. This is particularly relevant where the number of multiple events in a study is large as if patients with certain characteristics are more likely to have multiple events, the data could be skewed by this. On the other hand, studies that only report the first event are unable to measure the total burden of recurrent events on a population. In keeping with the fracture epidemiology literature, in this study, recurrent NHF episodes in the same patient over time were recorded as ‘two fractures, one patient’. Only 51 out of 2,632 (1.9%) patients had multiple fractures during the present study so the effect of multiple events is likely to be low.

In summary, this chapter has demonstrated the epidemiology of NHF. The data presented in this chapter CHAPTER 4.

CHAPTER 4
PREVALANCE AND PREDICTION OF NONUNION AFTER NECK OF HUMERUS FRACTURE

4.1 CHAPTER AIMS

The aims of this chapter were to determine the prevalence of nonunion after NHF and to identify patient and radiographic risk factors for nonunion.

4.2 INTRODUCTION

Nonunion is a serious complication of NHF. Its prevalence is uncertain because of a lack of epidemiological investigation in unselected populations, with rates from different centres ranging from 1.1% to 20%(1, 3, 78, 79). It is an important cause of poor functional outcome following NHF, is readily diagnosed and may be preventable with appropriate, timely surgical intervention(3). Priority should therefore be given to developing a means of identifying patients at increased risk of developing this adverse outcome following a diagnosis of NHF. This in turn will provide a basis for patient selection in trials of surgical intervention.

Whilst it is plausible that fractures with wide displacement of the shaft in relation to the head of humerus are at increased the risk of nonunion, the value of radiographic predictors such as this, or other patient or injury characteristics has not been established. This chapter aims to determine the prevalence of nonunion after NHF and to identify patient and radiographic risk factors for nonunion.

4.3 METHODS

Database 1 was used to evaluate the outcome of humeral neck fractures and then to generate a mathematical model predicting nonunion. The setting, method of case ascertainment and demographic data collected is described in detail in CHAPTER 2.

An additional retrospective review of all case notes and fracture radiographs was made by the author (EBG) for the purposes of the present study and the following data were recorded:

4.3.1 **Radiographic data**

All available, adequate, initial post-injury radiographs were analysed, and a series of measurements were made by the author (EBG). The method used to make each measurement is shown below.

Humeral head angulation (Figure 4-1)

Line A: Superior margin of humeral head articular surface to inferior margin of humeral head articular surface.

Line B: Superior margin of glenoid to inferior margin of glenoid.

Line C: perpendicular to line B passing through apex of humeral head articular surface.

Humeral head angulation = angle (degrees) between line B and line C.

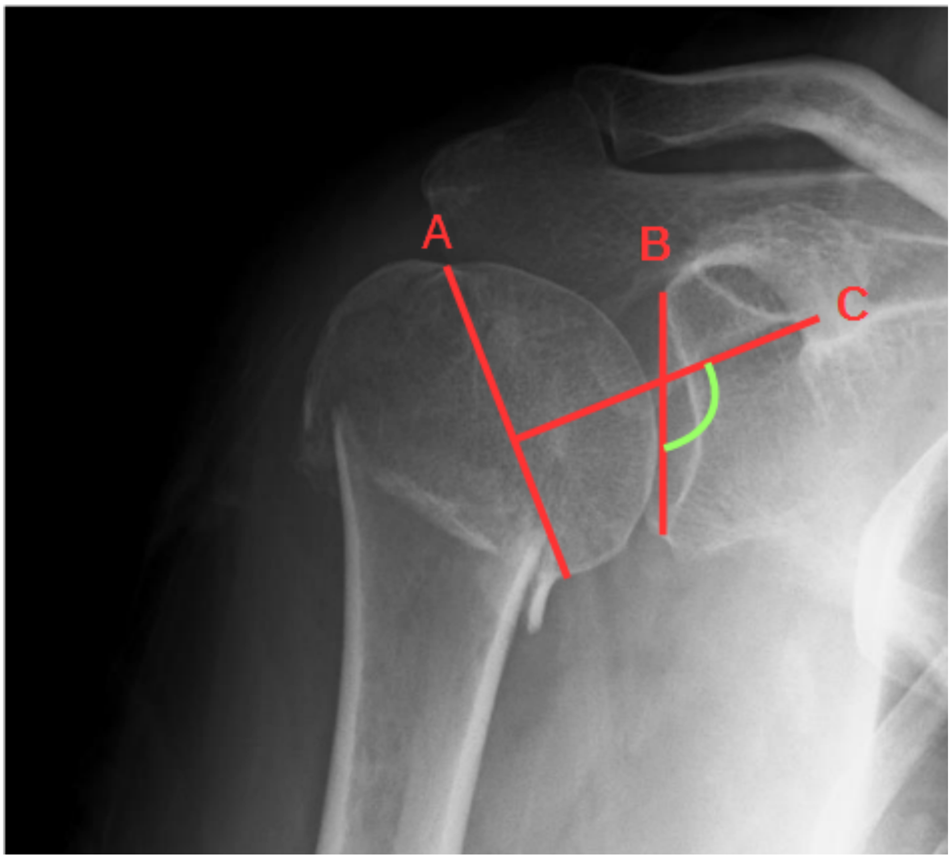


Figure 4-1 Humeral head angulation.

Fracture angle (Figure 4-2)

Line A: Long axis of humerus.

Line B: Level of fracture at lateral cortex of the humeral shaft to level of fracture at medial cortex of the humeral shaft.

Fracture angle = Angle (degrees) between line A and line B.

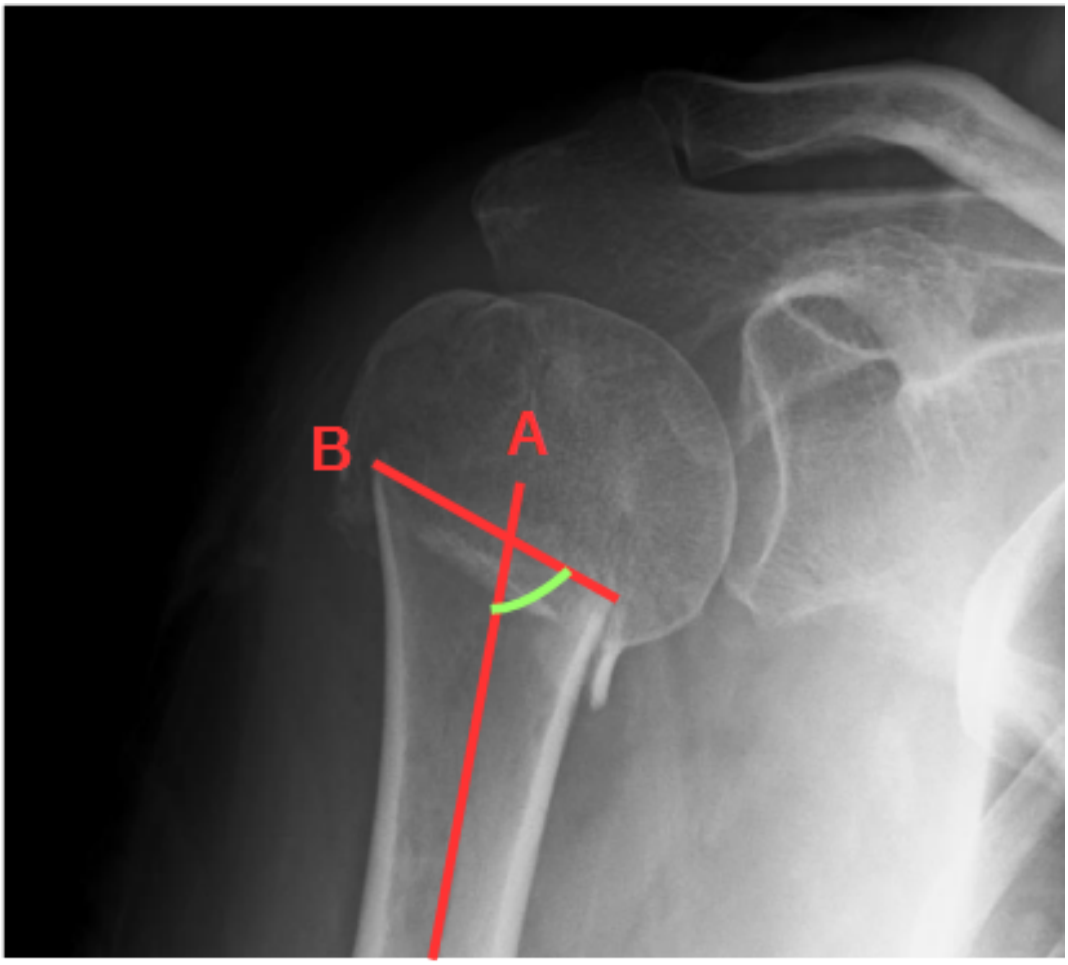


Figure 4-2 Fracture angle.

Fracture comminution Figure 4-3

Comminution present = greater than 2 main fracture fragments

Comminution absent = no greater than 2 main fracture fragments

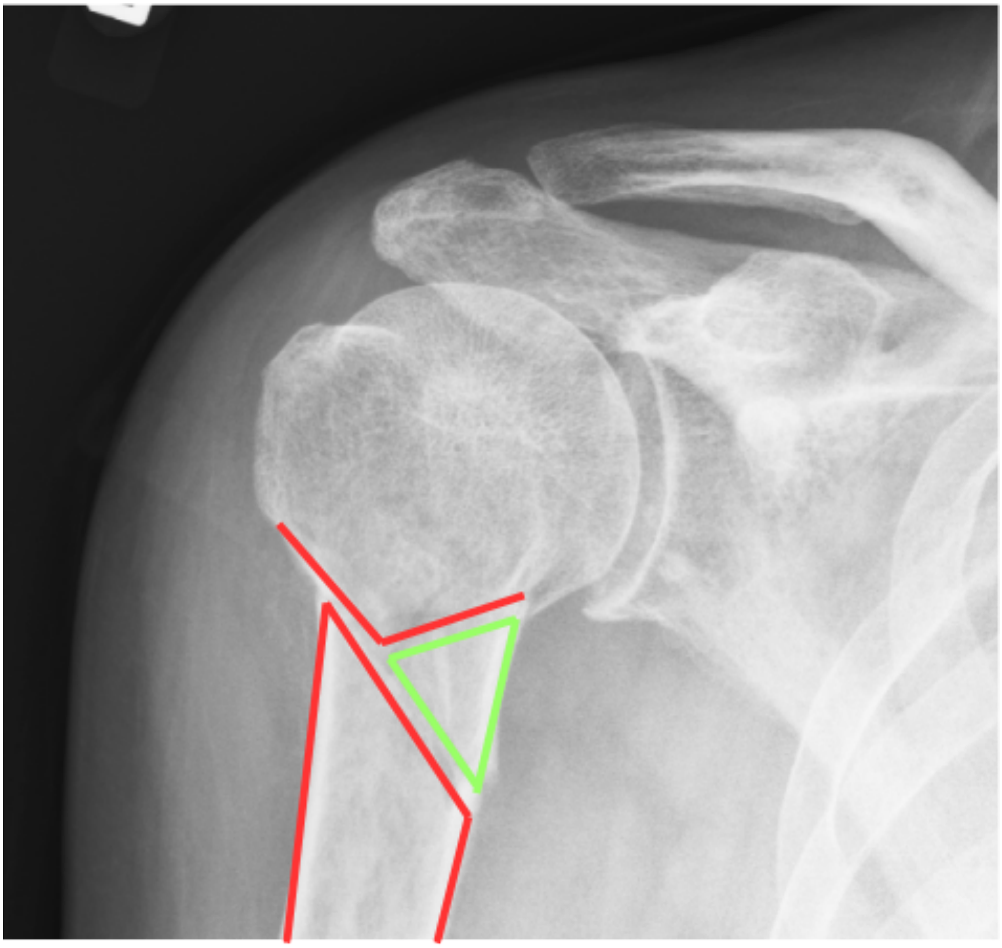


Figure 4-3 Example of a fracture with comminution present. The three main fracture fragments are highlighted.

Tuberosity involvement

Tuberosity involvement was classified as either present or absent depending on whether there was an associated fracture of the greater lesser or both tuberosities. Fractures with an associated tuberosity were further classified by tuberosity displacement (<1mm displacement was classified as ‘undisplaced and ≥1mm displacement was classified as ‘displaced’) and by the pattern of tuberosity involvement (neck plus greater tuberosity, neck plus lesser tuberosity or neck plus both tuberosities).

Humeral head-shaft translation (Figure 4-4 and Figure 4-5)

Line A: diameter (mm) of distal fragment at the level of the fracture

Line B: maximal translation (mm) of distal fragment in relation to proximal fragment at the level of the fracture.

Percentage translation = (line B / line A) x 100.

The percentage translation was measured on the AP and modified axial radiographs and the greater value was taken as the humeral head-shaft translation.

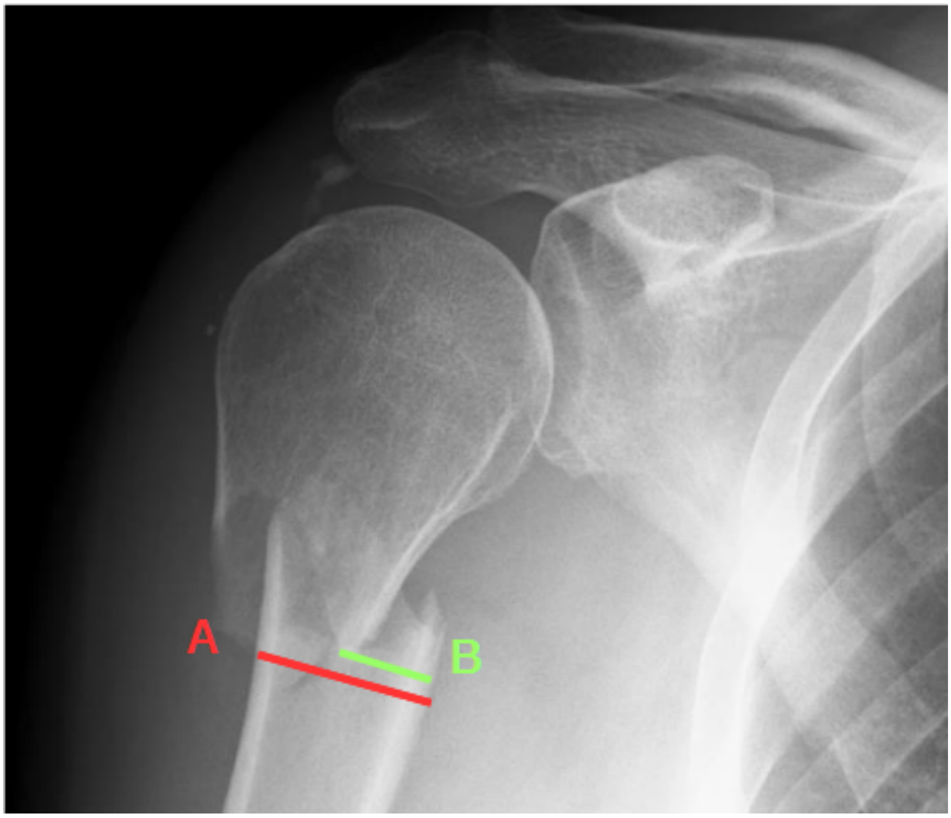


Figure 4-4 Humeral head-shaft translation (AP view).

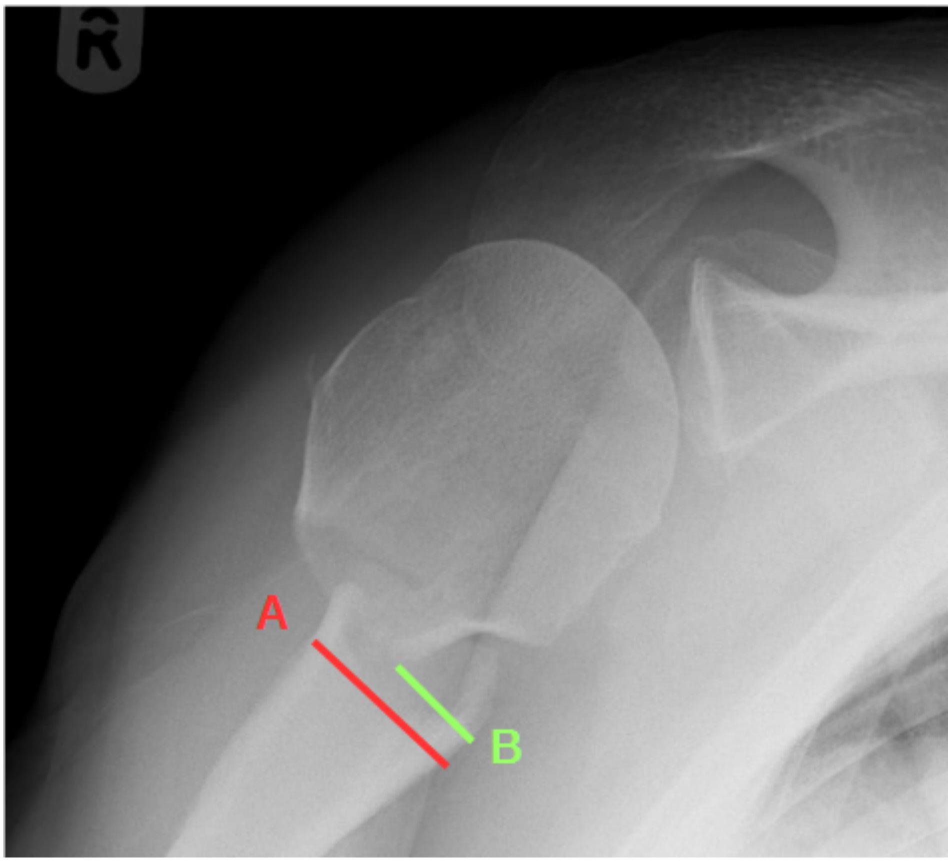


Figure 4-5 Humeral head-shaft translation (modified axial view).

Involvement of humeral diaphysis (Figure 4-6, Figure 4-7 and Figure 4-8)

Any fracture extending distally, beyond the inferior margin of the modified Muller's box was deemed to involve the humeral diaphysis.

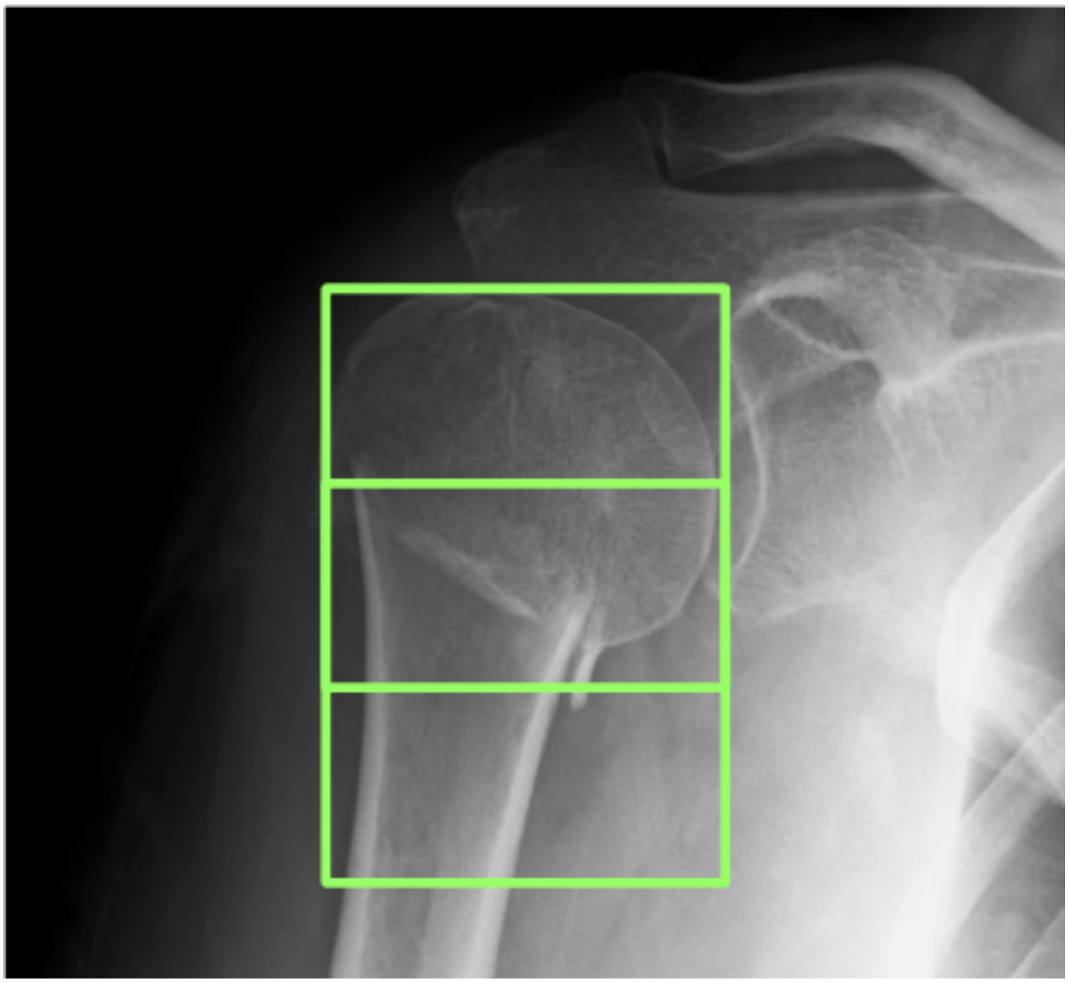


Figure 4-6 A NHF without diaphyseal involvement.

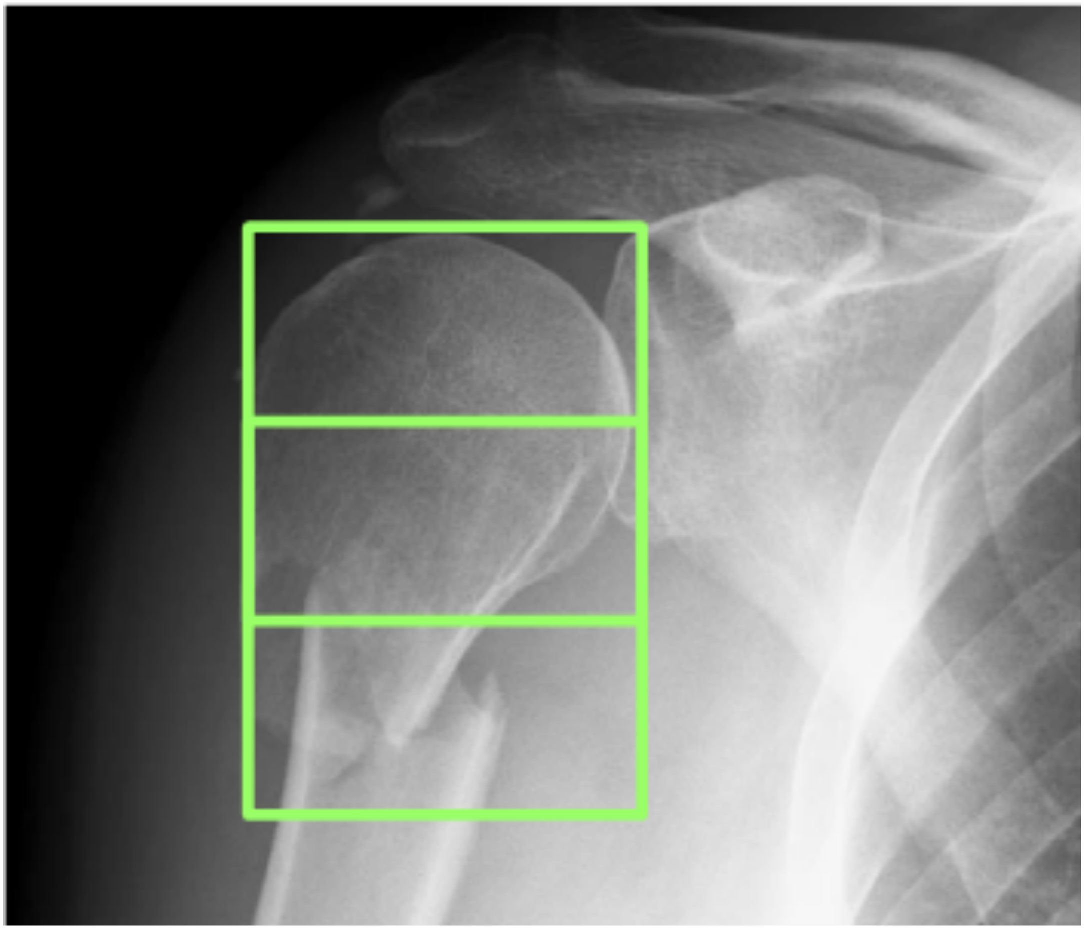


Figure 4-7 A NHF with extension into the distal third of the modified Mullers box but without diaphyseal involvement.

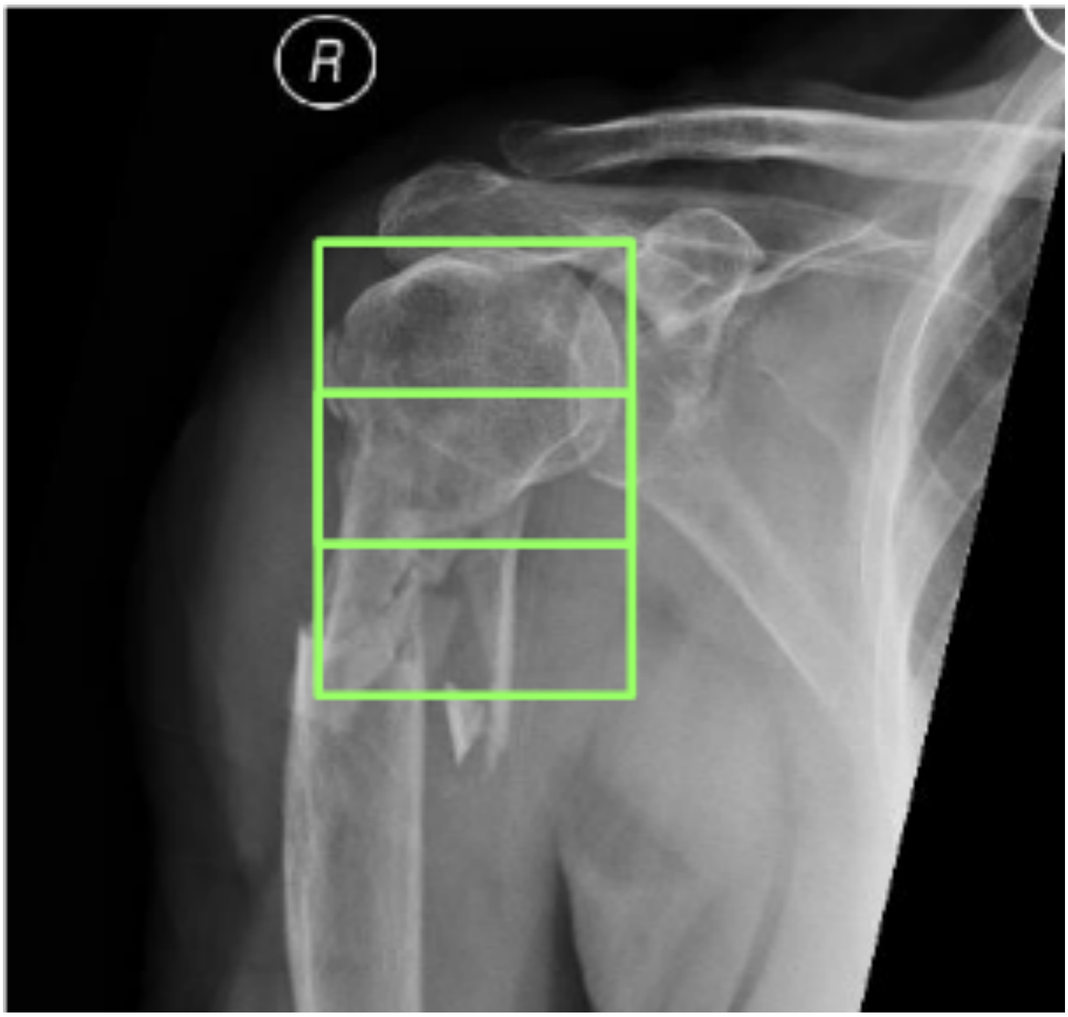


Figure 4-8 A NHF with extension outwith the with the modified Mullers box and diaphyseal involvement.

Separation between the two main fracture fragments (Figure 4-9and Figure 4-10)

Fractures with no overlap between two main fragments on either the AP or the modified axial radiograph were classified as ‘separated’. The remainder of fractures, including undisplaced and impacted fractures were classified as ‘not separated’.

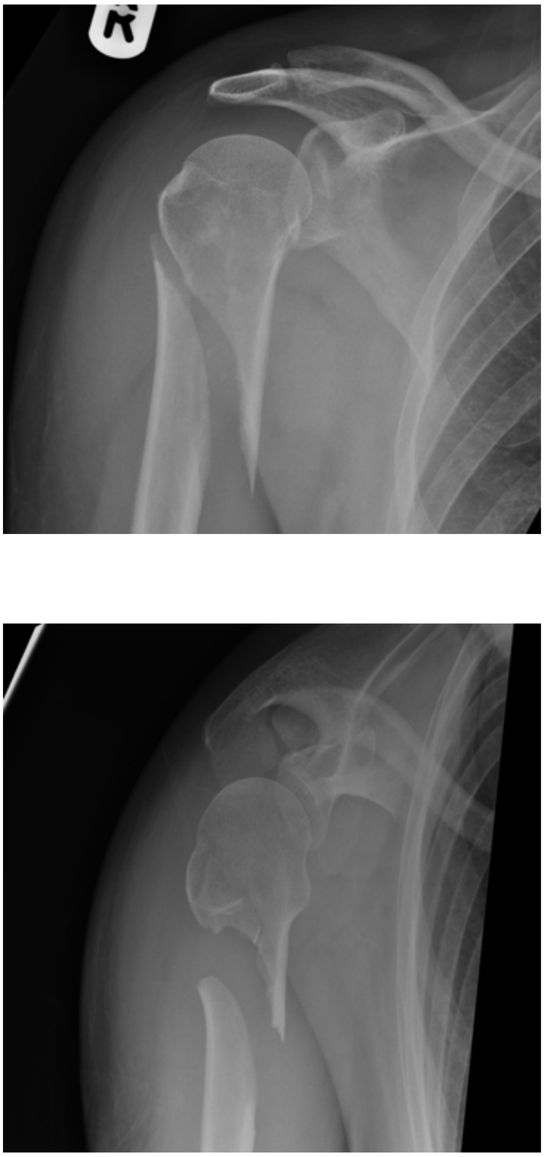


Figure 4-9 AP and modified axial radiograph of fracture with separation between the head and shaft fragments.

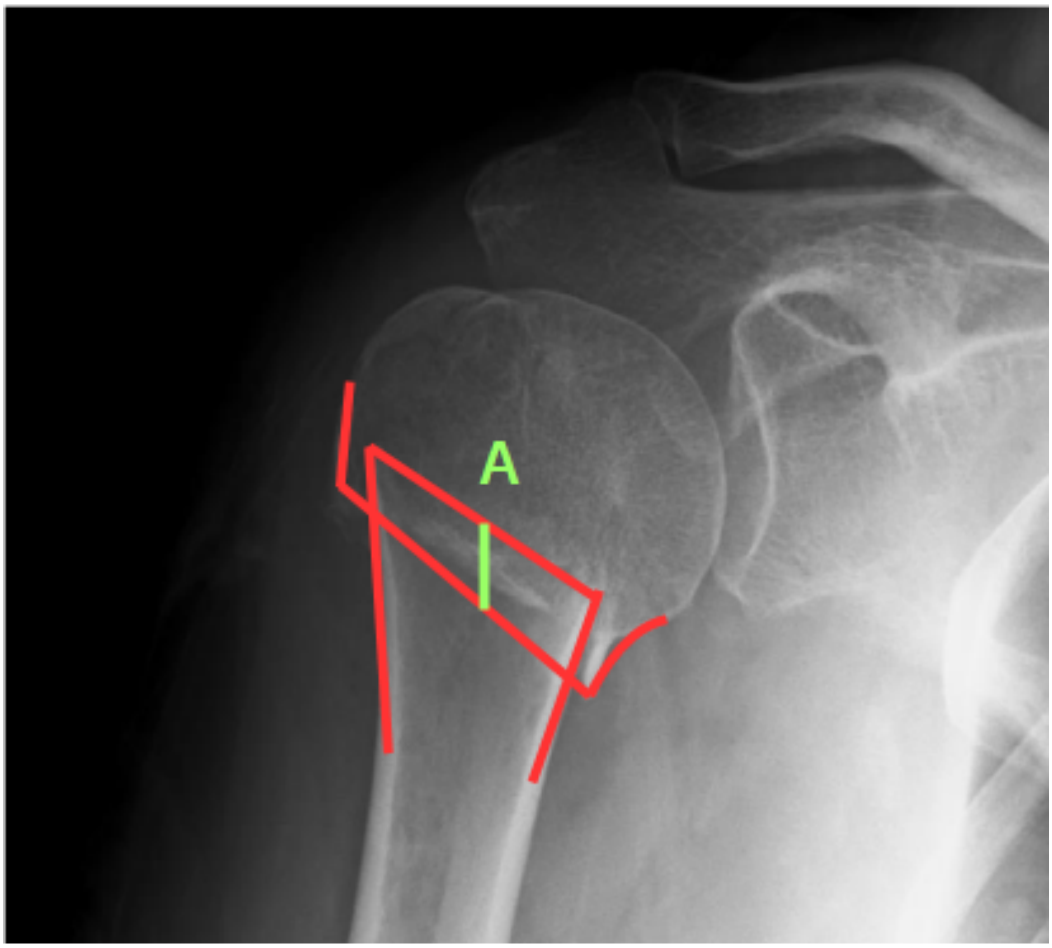


Figure 4-10 A fracture with no separation. There is impaction with overlap of the two principal fragments (B).

Glenoid height (Figure 4-11)

Line A: superior margin of glenoid to inferior margin of glenoid.

Glenoid height = length (mm) of line A.

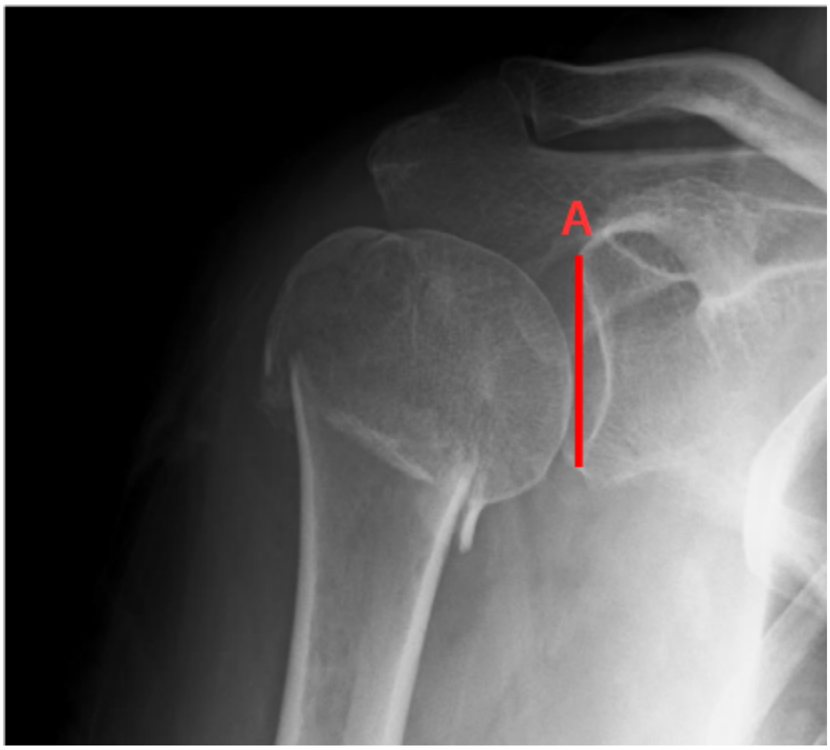


Figure 4-11 Glenoid height (A).

Length of intact medial calcar (Figure 4-12)

Line A: Superior margin of glenoid to inferior margin of glenoid (glenoid height).

Line B: Superior margin of humeral head articular surface to inferior margin of humeral head articular surface.

Line C: The intact medial calcar was the portion of intact bone between the inferior margin of the humeral head articular surface and the most proximal level at which the fracture line exits medially.

Line D: Length of medial calcar. Straight line between the inferior margin of the humeral head articular surface and the most proximal level at which the fracture line exited medially.

In order to account for radiographic magnification error, line D was expressed as a percentage of line A.

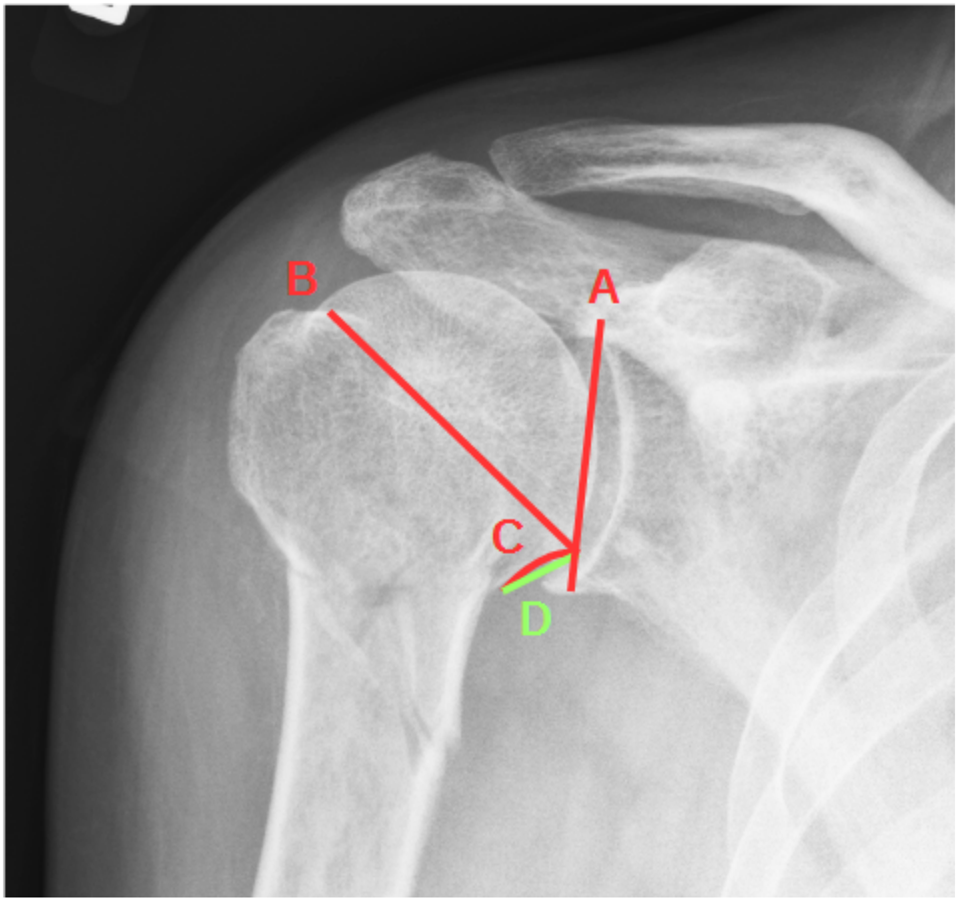


Figure 4-12 Length of intact medial calcar.

Length of medial cortex fracture (Figure 4-13)

Line A: Superior margin of glenoid to inferior margin of glenoid (glenoid height).

Line B: Superior margin of humeral head articular surface to inferior margin of humeral head articular surface.

Line C: Perpendicular to line A, at the level of the inferior margin of the humeral head articular surface.

Line D: Length of medial cortex fracture. Length of line running perpendicular from line C to most distal level at which the fracture line exited medially.

In order to account for radiographic magnification error, line D was expressed as a percentage of line A.

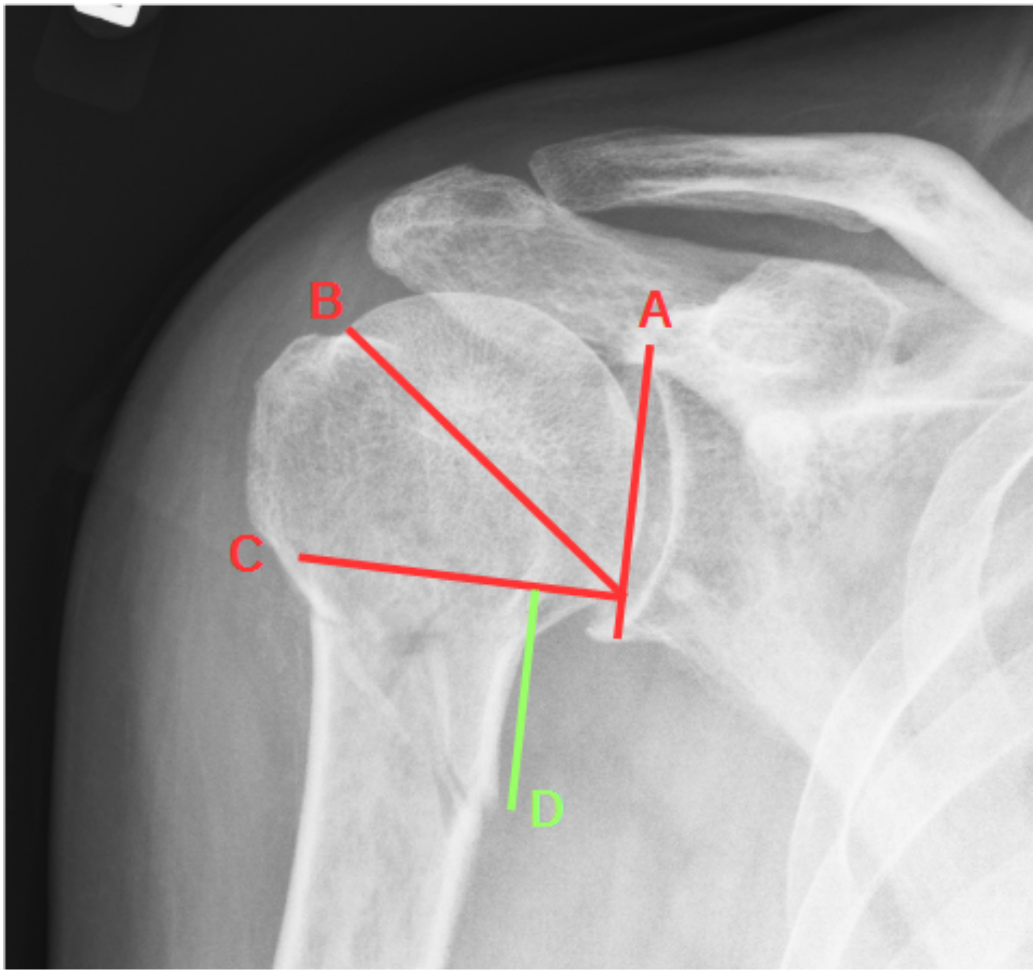


Figure 4-13 Length of medial cortex fracture.

Length of lateral cortex fracture (Figure 4-14)

Line A: Superior margin of glenoid to inferior margin of glenoid (glenoid height).

Line B: Superior margin of humeral head articular surface to inferior margin of humeral head articular surface.

Line C: Perpendicular to line A, at the level of the inferior margin of the humeral head articular surface.

Line D: Length of lateral cortex fracture. Length of line running perpendicular from line C to most distal level at which the fracture line exits laterally.

In order to account for radiographic magnification error, line D was expressed as a percentage of line A.

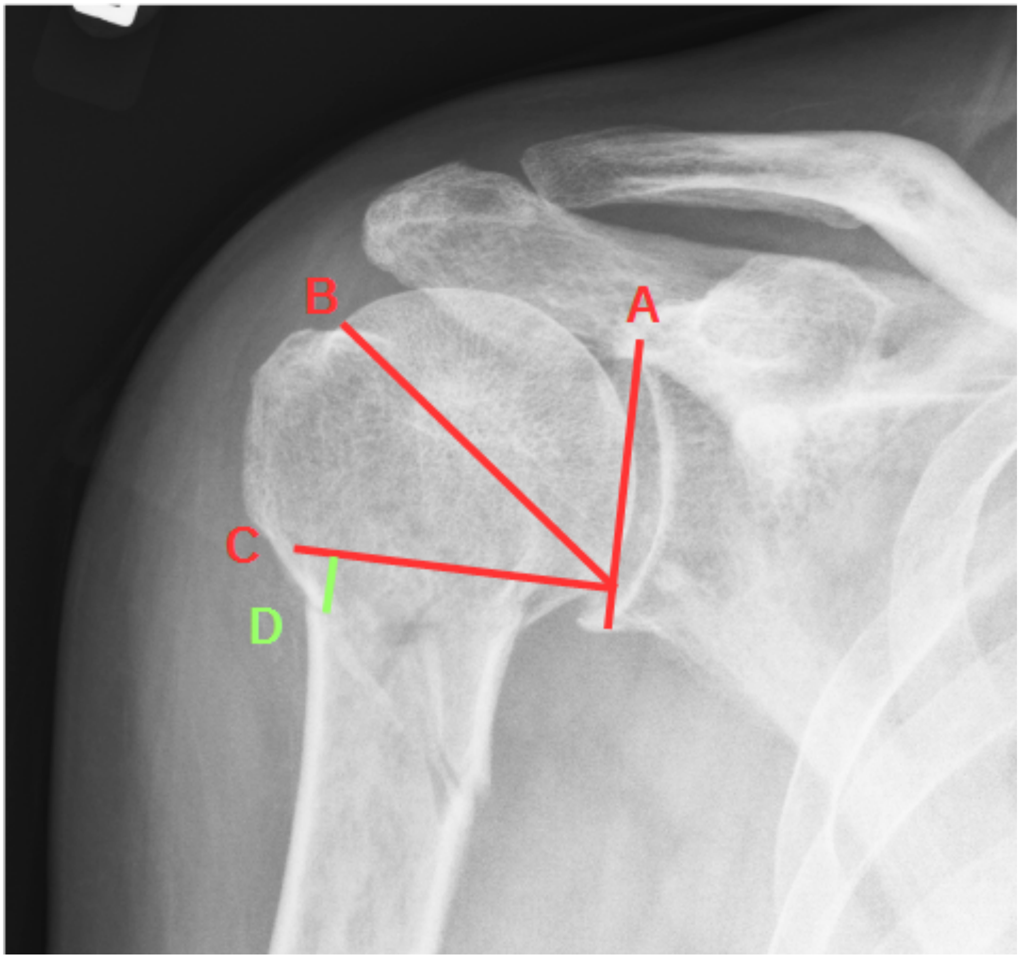


Figure 4-14 Length of lateral cortex fracture.

4.3.2 **Validation of the radiographic data**

For validation of the radiographic measurements, the study number of every fiftieth patient in the dataset was taken. The fracture radiographs of these patients were then re-examined by the author (EBG) without reference to the original database. Each of the measurements described in section 4.3.1 were recorded and entered into a new spreadsheet. The new spreadsheet was compared to the original dataset.

4.3.3 **Details of primary treatment decision**

The primary treatment decision (nonoperative or operative) was recorded.

4.3.4 **Details of surgery**

Details of primary or secondary surgery (if performed) were recorded. This included the date of surgery, type of surgery, and complications.

4.3.5 **Outcome data**

Fracture outcome was assessed by retrospective review of case notes and follow-up radiographs by EBG. A fracture was judged to be united when a patient had no or minimal pain, no or minimal functional limitation, no mobility at the fracture site, and trabeculation across the fracture on both views or, in those fractures which were displaced, when the lateral bone bridge is complete. Nonunion was judged to be present if there was absence of radiological union and any of ongoing pain, functional limitation or mobility at the fracture site three months or longer following injury.

4.3.6 **Mortality data**

Mortality data (including verification for death, date of death and cause of death) were checked by anonymised computerised linking with the Regional Death Registry records obtained from the General Registry Office for Scotland. Verification of death and date of death was also cross-checked manually in every patient with electronic hospital records. Survival was assessed from the date of the fracture until the date of death from any cause.

4.3.7 **Inclusion and exclusion criteria**

In addition to patients excluded from the epidemiological analysis, the following exclusions were made when evaluating outcome.

1. Patients who died within three months of sustaining their fracture were excluded deemed ineligible for outcome analysis as they were not at risk of developing nonunion.
2. Patients with an associated glenohumeral dislocation were excluded as the vast majority of these patients underwent either manipulation under anaestheisia or primary surgical fixation.
3. Patients who underwent primary surgical treatment were excluded from the outcome analysis, as this precluded the natural history of the fracture.
4. Patients who defaulted from follow-up within three months of sustaining their fracture whose fracture had not already healed were excluded from the outcome analysis as it was not possible to confirm the presence or absence of fracture union in this group.

4.3.8 **Missing data**

Depending on the nature of missing data, certain patients were excluded from certain outcome analyses.

1. No post-injury radiographs available for retrospective analysis. These patients were excluded from all outcome analyses, as fracture outcome is meaningless without being able to define the nature of the fracture at presentation.

2. Patients with other missing input data were excluded from the analysis of the predictive significance of that data. For example, patients with no details for an individual radiographic measurement were excluded from the analysis of that measurement as a factor predictive of nonunion.

4.3.9 **Statistical analysis**

Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington) and SPSS version 21.0 (SPSS, Chicago, Illinois) were used to undertake statistical analysis. For the purposes of validation of the radiographic measurements, the percentage agreement for binary variables, and correlation between the two databases were calculated.

Bivariate binary logistic regression was used to estimate the effect of candidate patient- related, injury-related risk and radiographic factors on the development of nonunion. The analysis was performed with independent variables classified as either continuous or categorical data. The relationship of continuous variables with probability of nonunion was examined and tested as either linear or quadratic, depending on whether or not the quadratic term was significant. A linear relationship is a statistical term used to describe a straight-line relationship between a variable and a constant. Linear relationships can be expressed either in a graphical format or as a mathematical equation of the form $y = ax + b$. A quadratic relationship expressed on a graph forms a parabola, which looks like a dip or a valley and the relationship between two variables can be expressed as a mathematic equation of the form $y = ax^2 +bx + c$.

All radiographic that were significantly predictive of nonunion on bivariate analysis were included in a stepwise multivariate regression analysis (with use of forward conditional methodology) to identify the radiographic factors that were independently predictive of nonunion. Stepwise multivariate regression is a method of regressing multiple variables while simultaneously removing those that aren't important. It essentially does multiple regression a number of times, each time removing the weakest correlated variable. This analysis provides the solution to the equation (Armitage and Berry 1994):

$$y = a + b_1x_1 + b_2x_2 + b_3x_3 + \ldots.. + b_nx_n$$

Where y is the outcome, a and b_1 to b_n are the constants and x_1 to x_n are the input variables. Logistic regression was used as the outcome is binary: nonunion or healed fracture. This involves the transformation of the probability p of each outcome using the logistic function:

$$y = \log(p/1\text{-}p)$$

The 'best fit' solution is found where the difference between observed and expected values are minimized. The analysis was performed in a forward stepwise fashion. Thus input variables are added to the equation one at a time, in an order based upon their significance adjusted for those already added. Those variables significantly reducing the difference between observed and expected outcomes are retained in the equation and those that have no significant effect are deleted. The Hosmer-Lemeshow goodness-of-fit statistic was used to judge the predictive quality of the final model. The Wald chi-square test was used to assess the significance of the independent predictors of nonunion in the final model.

Using this model, the risk factor scores for an individual patient and their regression coefficients (B) can be used to calculate a logit value (logit[p]) for the probability (p) of nonunion. The predicted probability of nonunion can be computed for each patient using the following conversion equation:

$$\text{probability nonunion} = \exp^{\text{logit(y)}} / (1 + \exp^{\text{logit(y)}}$$

The value of exp(B) (the odds ratio) for each variable was estimated to allow quantification of the magnitude of the effect size of a one-unit change in the variable on the risk of nonunion when adjusted for other variables.

Classification tables of predicted and actual outcomes were used to estimate the sensitivity, specificity, positive predicted value, negative predicted value and overall percentage of correct predictions for the model at different thresholds of the estimated probability of nonunion. The number-needed-to-treat value (NNT) – the number of patients who would need one operation to prevent a single nonunion – was also assessed at each probability threshold to assess the implications of adopting a policy of primary operative intervention for these fractures.

Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability of the model to predict nonunion. The area under the ROC curve can range from 0.5, indicating a test with no accuracy in distinguishing whether a patient will go onto nonunion, to 1.0 where the test is perfectly accurate in identifying all patients with nonunion. For all of the analyses, a two-tailed p value of <0.05 was considered statistically significant.

4.4 RESULTS

4.4.1 Outcome study population

Of the 2,683 fractures included in the epidemiological section of the study, 132 occurred in patients who died within 3 months of injury. These patients were not at risk of nonunion and were therefore ineligible for outcome analysis. This left 2,551 eligible fractures in patients who survived beyond 3 months of their injury.

Of the 2,551 fractures which were eligible for outcome analysis, 274 underwent primary surgical fixation or had an associated glenohumeral dislocation and were therefore excluded. 441 fractures either had post injury radiographs were unavailable or inadequate or defaulted from follow-up prior to the confirmation of fracture union and were therefore also excluded. Thus 1,802 out of 2,551 (70.1%) eligible factures were included in the outcome analysis.

The 1,802 fractures occurred in 1,778 patients. 24 of the patients who were included in the outcome analysis either had bilateral simultaneous fractures or two fractures at different times during the study. There were 448 (24.9 percent) males and 1354 (75.1 percent) females. The median age of all patients was 72 years (IQr, 58 – 81) with a range from 16 years to 103 years. The median age of females was 74 years (IQr, 63 – 81 yrs) and the median age of males was 63 years (IQr 50 – 75 years).

4.4.2 Validation of the radiographic data

The validation of the radiographic data is shown in Table 4-1.

Radiographic variable	Percentage agreement (%)	Correlation (r)
Humeral head angulation	Continuous variable	0.89
Fracture angle	Continuous variable	0.73
Fracture comminution	86.5	0.70
Tuberosity involvement	81.1	0.62
Tuberosity displacement	83.4	0.52
Humeral head-shaft translation	Continuous variable	0.87
Involvement of humeral diaphysis	97.3	0.70
Separation between the two main fracture fragments	94.6	0.64
Length of intact medial calcar	Continuous variable	0.73
Length of medial cortex fracture	Continuous variable	0.75
Length of lateral cortex fracture	Continuous variable	0.70

Table 4-1 Validation of the radiographic data.

4.4.3 Prevalence of nonunion

Of the 1,802 patients included in the outcome analysis, 128 developed nonunion, representing a risk of 7.1 percent (95% confidence interval, 5.9 percent to 8.3 percent).

4.4.4 Univariate analysis

Nonunion was described with respect to patient age, gender, mode of injury, social deprivation and the radiographic parameters described in section 4.3.1.

Patient age

The median age of patients whose fractures went on to heal was 72 years (IQr, 59 – 80) and the median age of patients whose fracture failed to unite was 71 years (IQr; 59 – 82 years). Figure 4-15 indicates fracture outcome according to age at the time of fracture. The risk of nonunion in patients aged 40 years and under was approximately 2 percent and the risk of nonunion in all other age groups was between 6 and 10 percent (Figure 4-16). Age was not predictive of nonunion on univariate analysis (p = 0.487, Bivariate binary Logistic Regression).

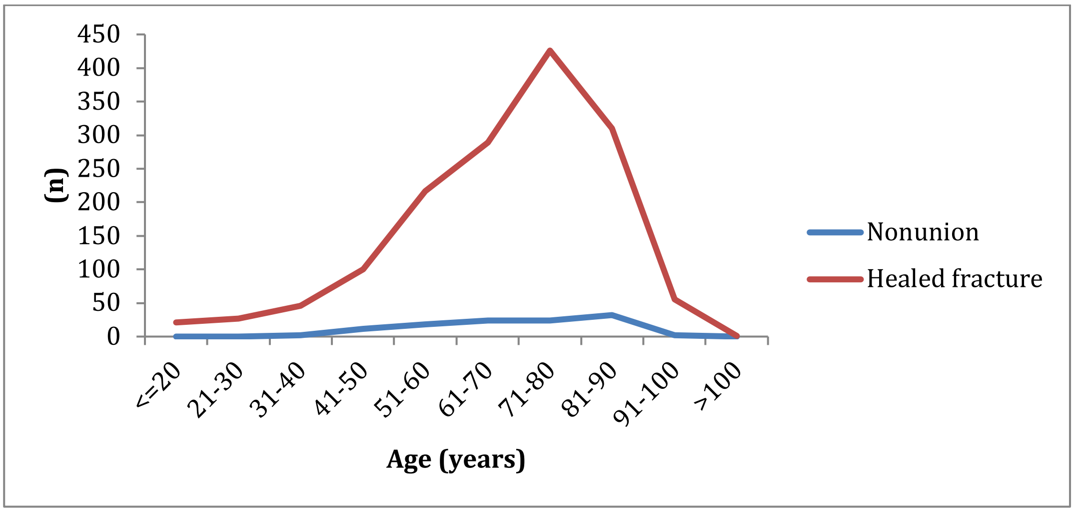


Figure 4-15 Frequency of nonunion according to patient age.

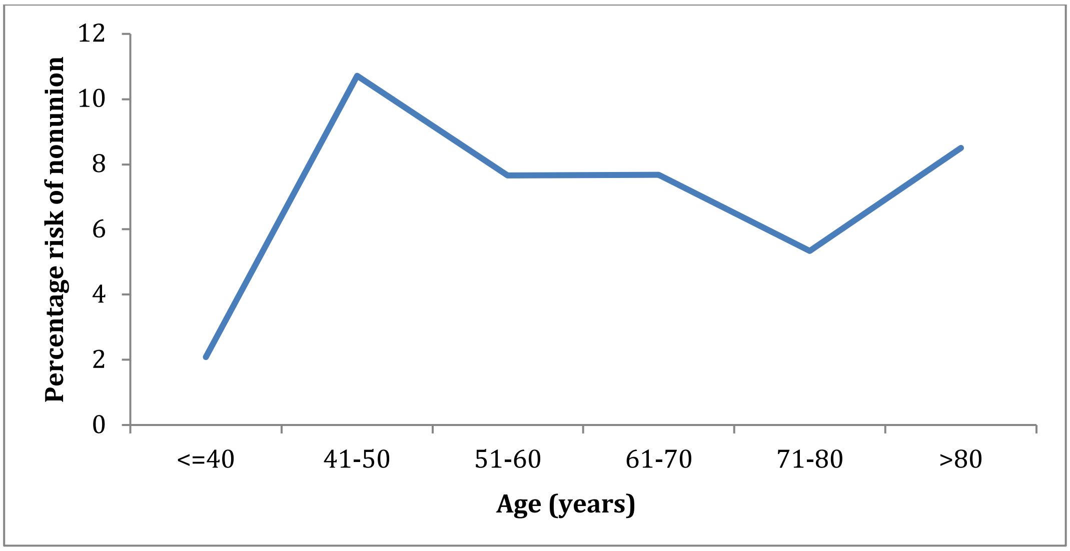


Figure 4-16 Percentage risk of nonunion according to patient age.

Gender

39 out of 448 (8.7 percent) males developed nonunion and 89 out of 1354 (6.6 percent) females developed nonunion. Gender was not predictive of nonunion on univariate analysis (p = 0.129, Bivariate binary logistic regression).

Mode of injury

The mode of injury was not predictive of nonunion on univariate analysis (p = 0.708, Bivariate binary logistic regression). Figure 4-17indicates fracture outcome according to mode of injury.

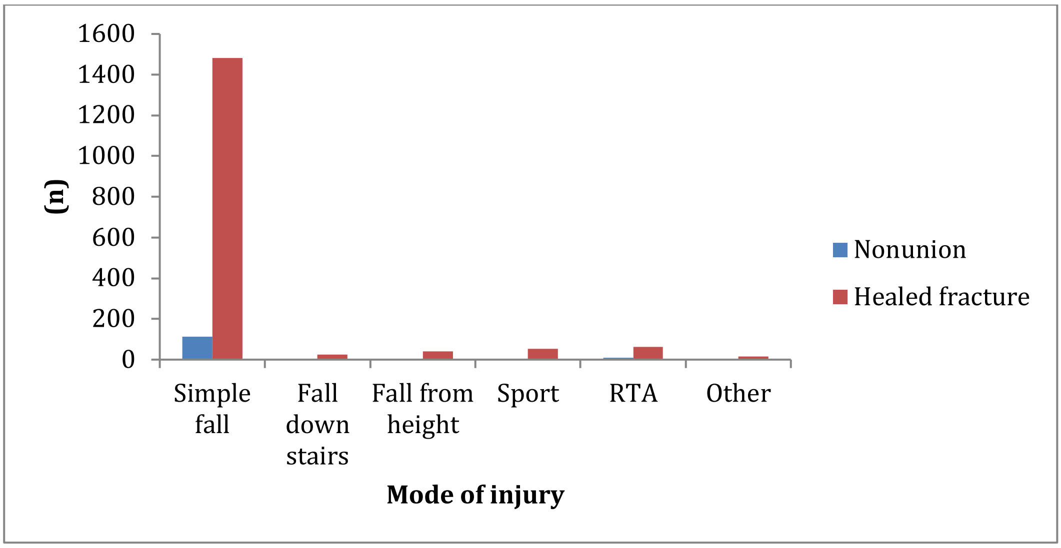


Figure 4-17 Frequency of nonunion according to mode of injury.

Social deprivation

Worsening social deprivation was predictive of nonunion on univariate analysis (p = 0.033, Bivariate binary logistic regression). Patients in deprivation quintiles 3, 4 and 5 had a statistically significant reduced risk of nonunion compared to their counterparts in deprivation quintile 1 (p = 0.012, p = 0.039, p =0.002 respectively, Bivariate binary logistic regression). There was a trend towards reduced risk of nonunion in patients in deprivation quintile 2 compared to deprivation quintile 1 but this was not statistically significant (p = 0.060, Bivariate binary logistic regression) (Figure 4-18).

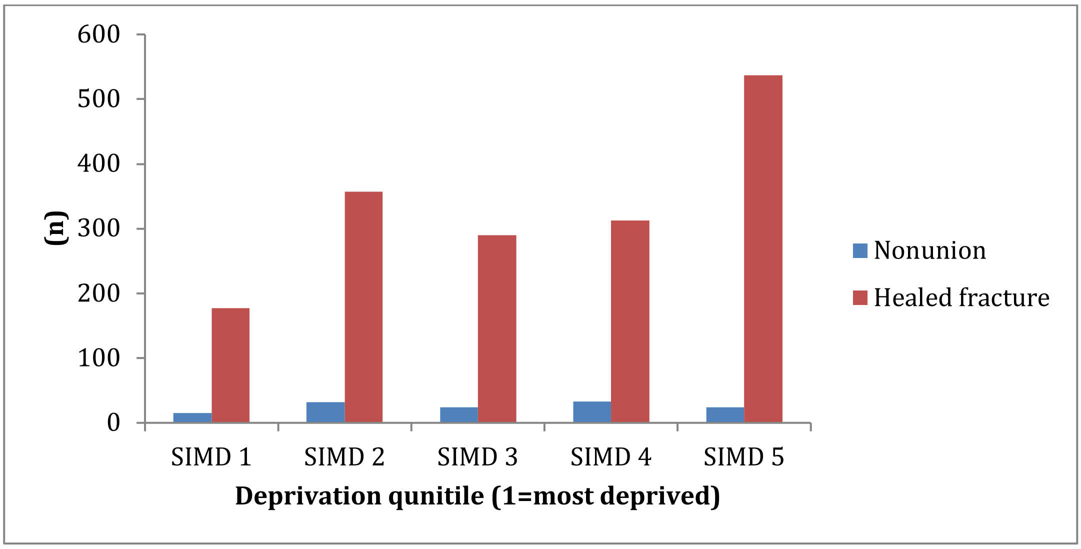


Figure 4-18 Frequency of nonunion according to deprivation quintile.

Radiographic measurements

Humeral head angulation

The humeral head angulation was between 100 and 150 degrees for the vast majority of fractures. The fit from the quadratic regression was not significantly better that from the linear regression indicating there was an approximately linear relationship between humeral head angulation and the logit of the risk of nonunion. Decreasing humeral head angulation was predictive of nonunion on univariate analysis ($p < 0.001$, Bivariate binary logistic regression). Figure 4-19 indicates fracture outcome according to humeral head angulation. Below 90 degrees of humeral head angulation, approximately 50 percent of fractures went on to nonunion (Figure 4-20). Only 3 fractures with a humeral head angulation of over 140 degrees did not heal.

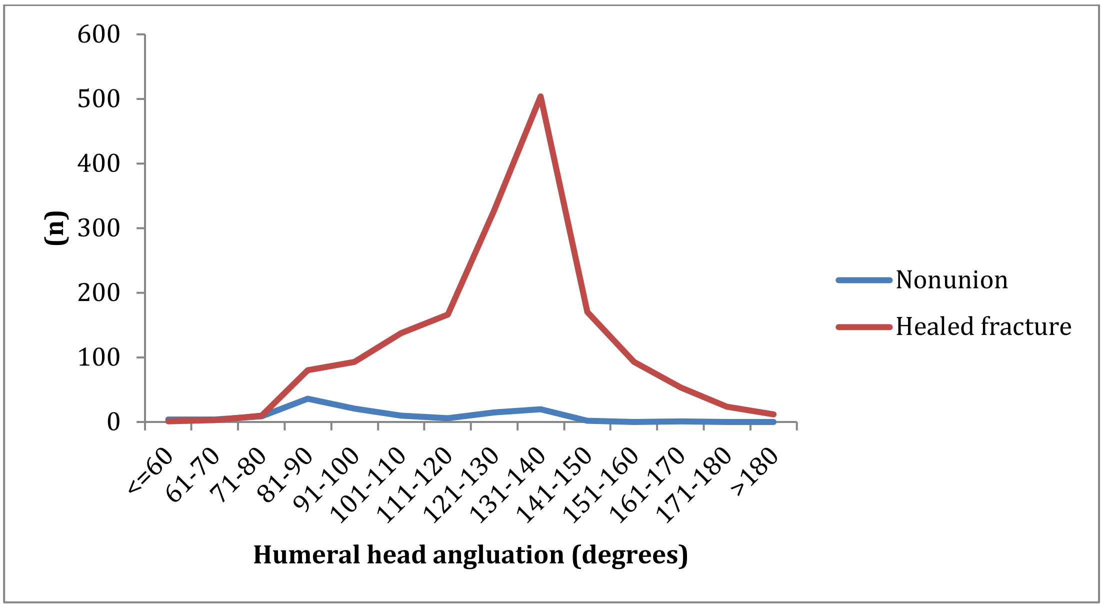


Figure 4-19 Frequency of nonunion according to humeral head angulation.

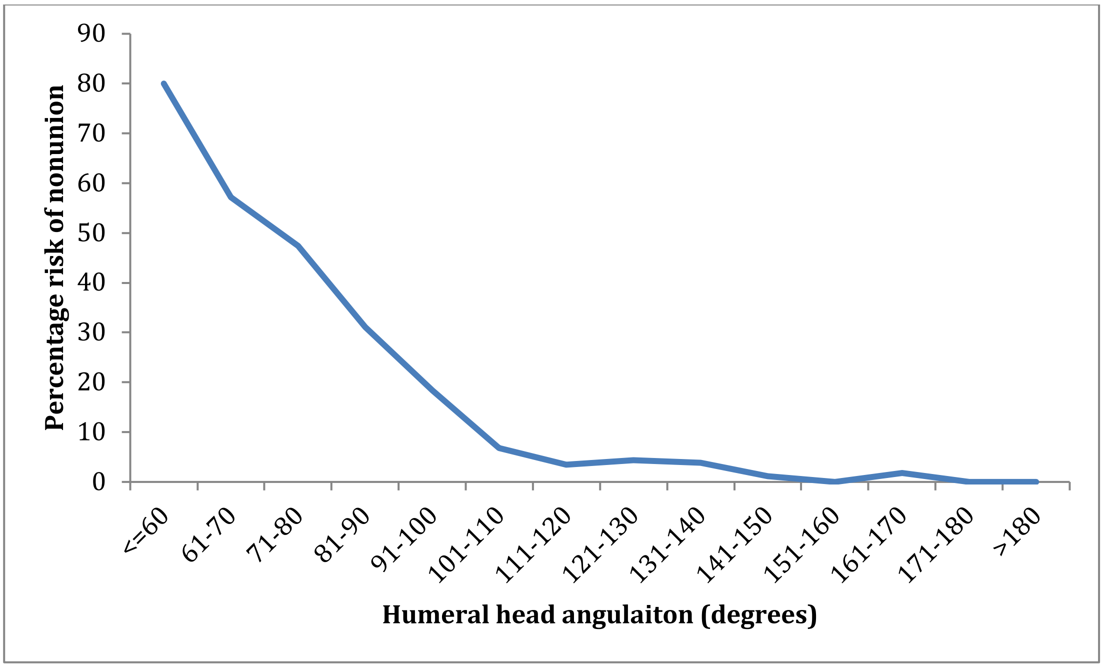


Figure 4-20 Percentage risk of nonunion according to humeral head angulation.

Fracture angulation

The fit of the quadratic model was significantly better than that of the linear model and therefore the relationship between fracture angulation and nonunion was non linear. There was an increased risk of nonunion as the fracture angle both increased or decreased from 90 degrees ($p < 0.001$, Bivariate binary logistic regression). The vast majority of fractures had a fracture angulation of between 70 and 100 degrees and the risk of nonunion was approximately 5 percent for these fractures (Figure 4-21) (Figure 4-22).

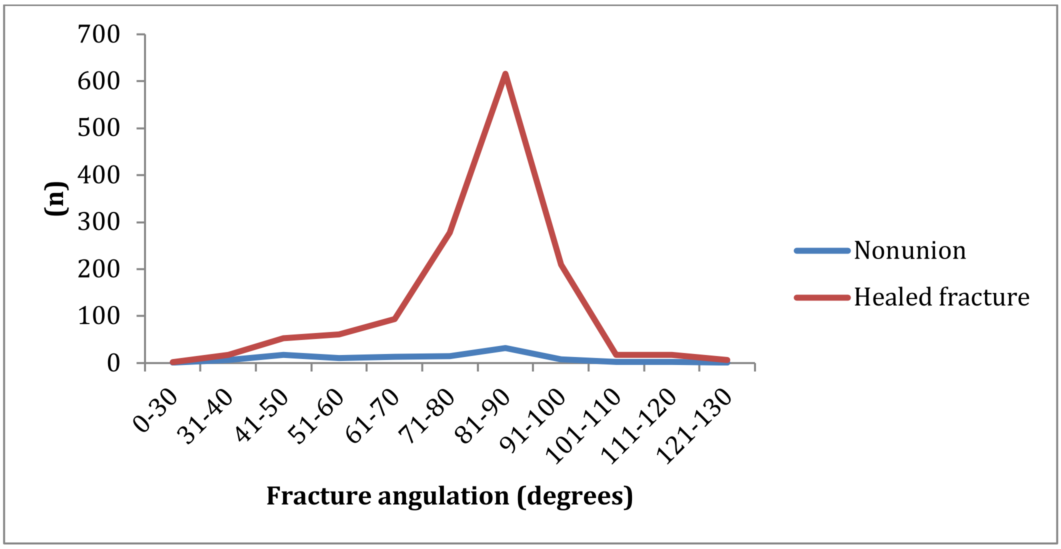


Figure 4-21 Frequency of nonunion according to fracture angulation.

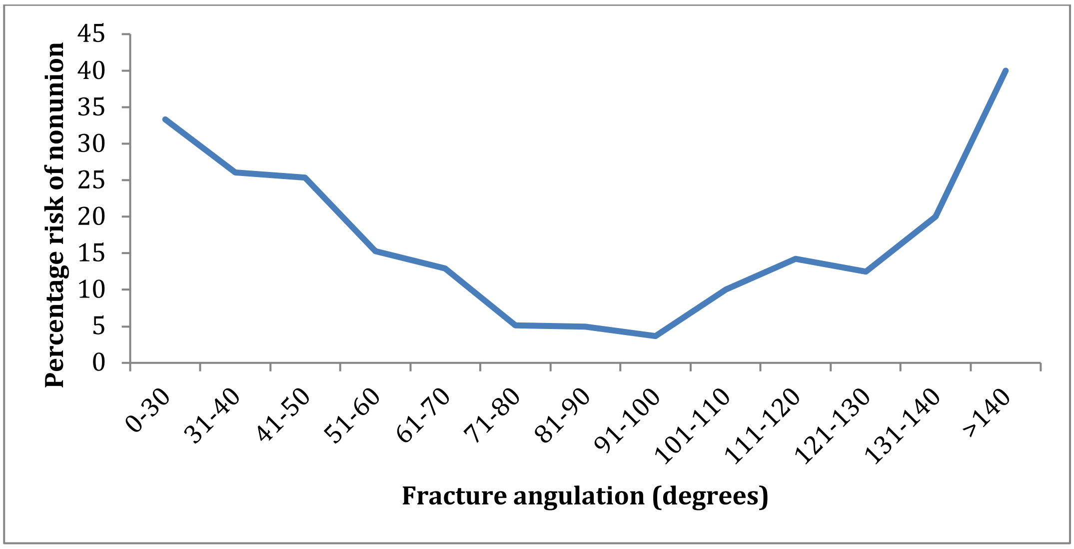


Figure 4-22 Percentage risk of nonunion according to fracture angulation.

Fracture comminution

Fracture comminution was predictive of nonunion on univariate analysis ($p < 0.001$, Bivariate binary logistic regression). Figure 4-23 indicates outcome according to fracture comminution.

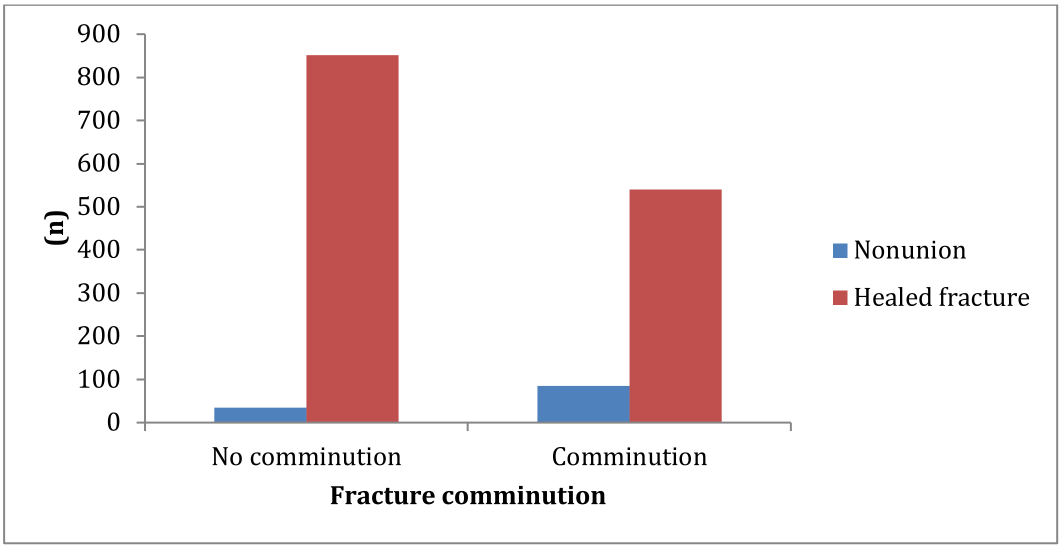


Figure 4-23 Frequency of nonunion according to fracture comminution.

Tuberosity involvement

Absence of tuberosity involvement was predictive of nonunion on univariate analysis (*p* < 0.001, Bivariate binary logistic regression) (Figure 4-24). The risk of nonunion for NHF involving either or both of the tuberosities was low (approximately 3 percent).

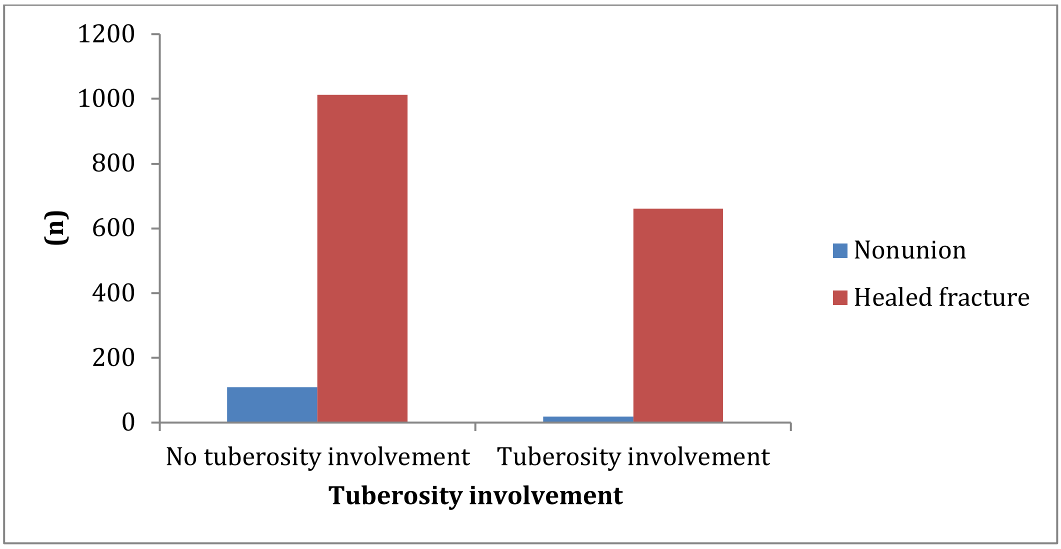


Figure 4-24 Frequency of nonunion according to tuberosity involvement.

Humeral head-shaft translation

The fit from the quadratic regression was not significantly better than from the linear regression indicating there was an approximately linear relationship between humeral head-shaft translation and the logit of the risk of nonunion. Increasing humeral head-shaft translation was predictive of nonunion on univariate analysis ($p < 0.001$, bivariate binary logistic regression) (Figure 4-25). Figure 4-26 shows the percentage risk of nonunion according to the humeral head-shaft translation. The vast majority of fractures had a humeral head-shaft translation of under 25 percent and the risk of nonunion was low (under 5 percent) in this group. A small number of fractures were completely off-ended with greater than 100 percent humeral head-shaft translation. This risk of nonunion was high (over 50 percent) for these fractures. A third group with moderate humeral head-shaft translation (over 25 percent but not completely off-ended) had an intermediate risk of nonunion (approximately 20 percent).

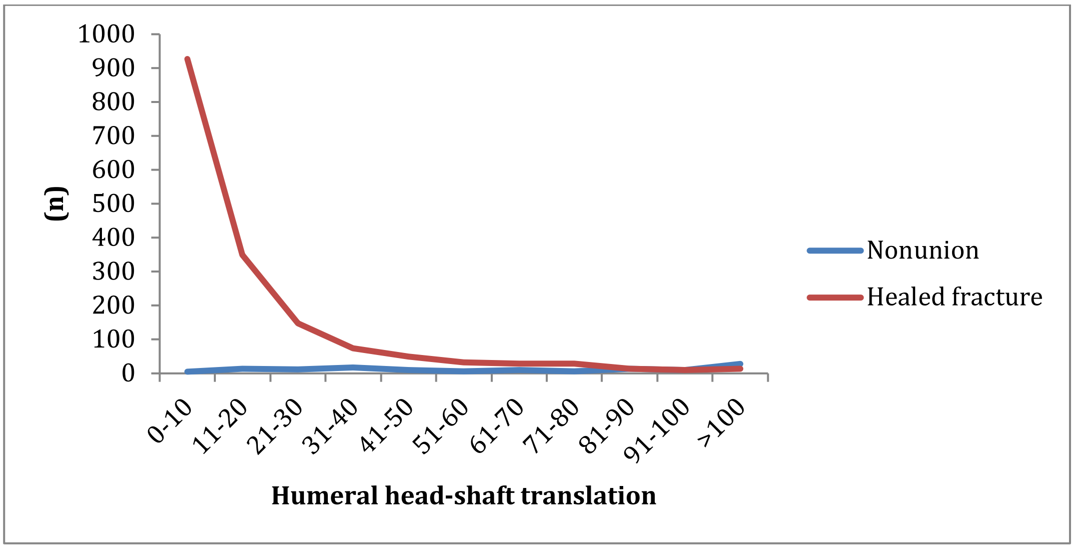


Figure 4-25 Frequency of nonunion according to humeral head-shaft translation.

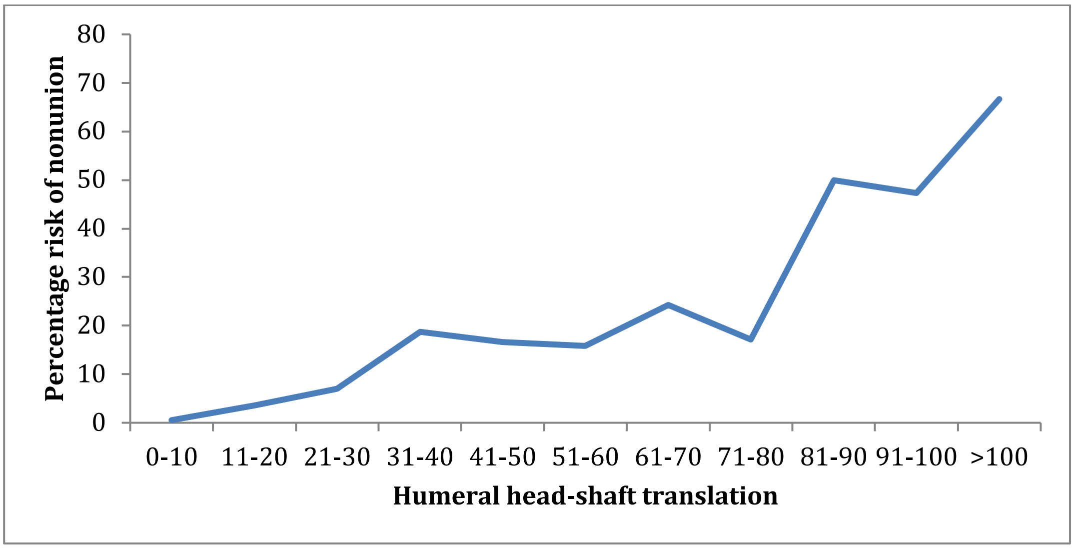


Figure 4-26 Percentage risk of nonunion according to humeral head-shaft translation.

Involvement of humeral diaphysis

62 out of 1802 fractures involved the humeral diaphysis, 17 of which developed nonunion. Humeral diaphyseal involvement was predictive of nonunion on univariate analysis (p < 0.001, bivariate binary logistic regression). Figure 4-27 indicates outcome according to humeral diaphyseal involvement.

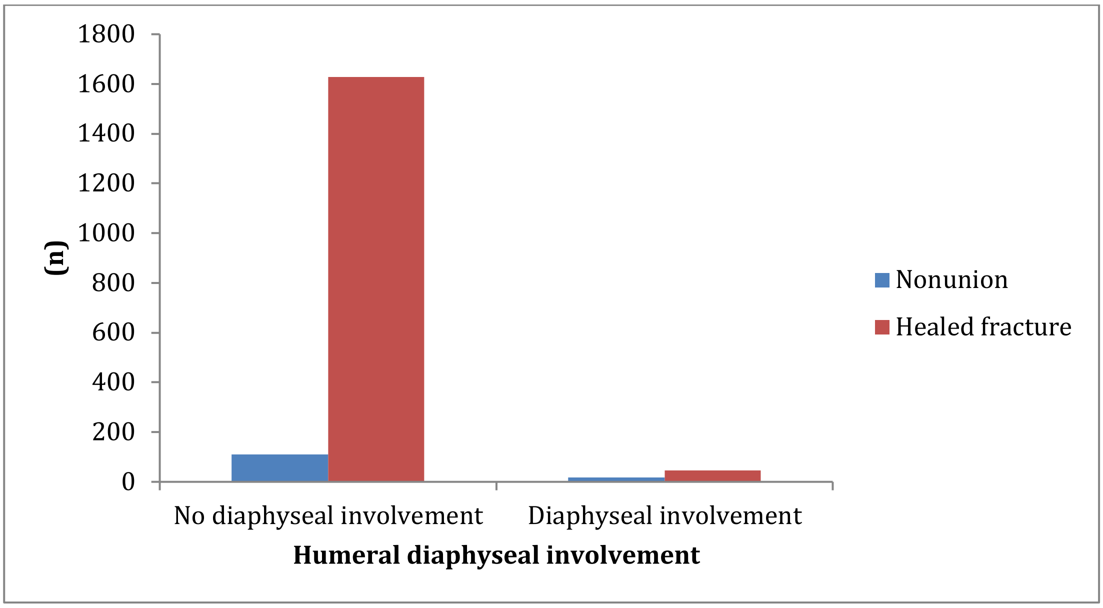


Figure 4-27 Frequency of nonunion according to involvement of the humeral diaphysis.

Humeral head-shaft impaction or separation

Separation between the two main fracture fragments was predictive of nonunion on univariate analysis ($p < 0.001$, Bivariate binary logistic regression). Figure 4-28 indicates outcome according to separation.

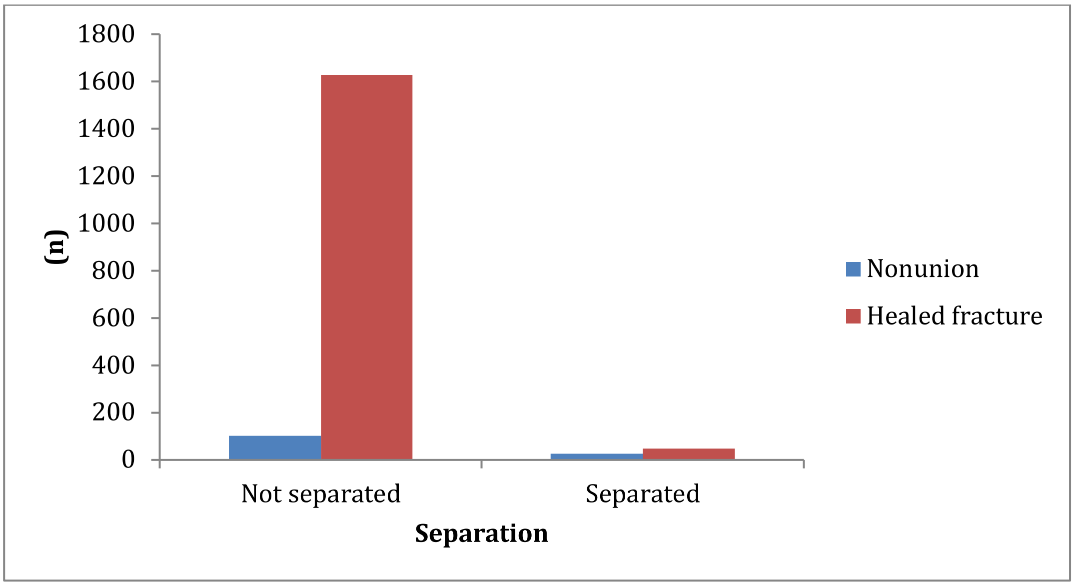


Figure 4-28 Frequency of nonunion according to separation of the two main fracture fragments.

Length of intact medial calcar

Fractures involving the humeral diaphysis were excluded from this section of the analysis. There was a linear relationship between length of the intact medial calcar and the risk of nonunion. Increasing length of intact medial calcar was associated with nonunion ($p < 0.001$, Bivariate binary logistic regression) (Figure 4-29) (Figure 4-30).

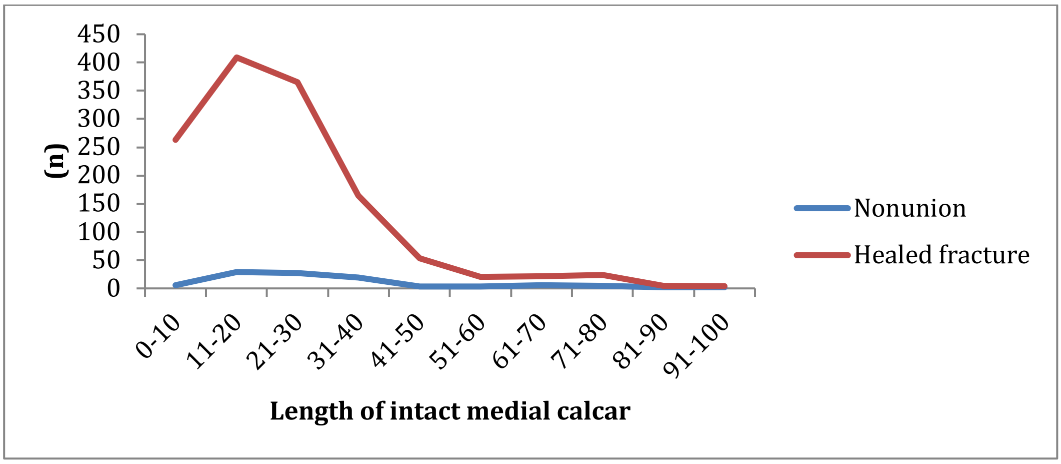


Figure 4-29 Frequency of nonunion according to length of intact medial calcar.

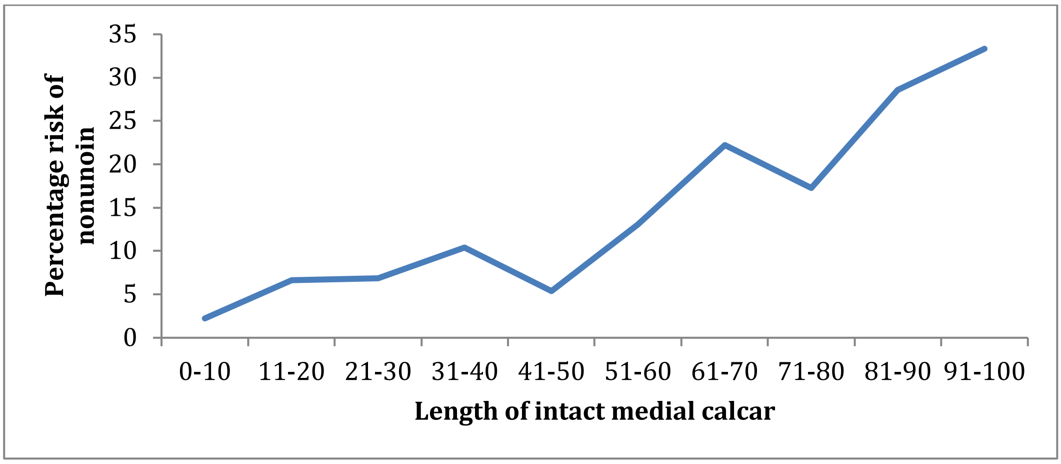


Figure 4-30 Percentage risk of nonunion according to length of intact medial calcar.

Length of medial cortex fracture extension

Fractures involving the humeral diaphysis were excluded from this section of the analysis. There was an approximately linear relationship between length of the medial cortex fracture extension and the risk of nonunion. Increasing length of the medial cortex fracture extension was associated with nonunion ($p < 0.001$, Bivariate binary logistic regression) (Figure 4-31) (Figure 4-32).

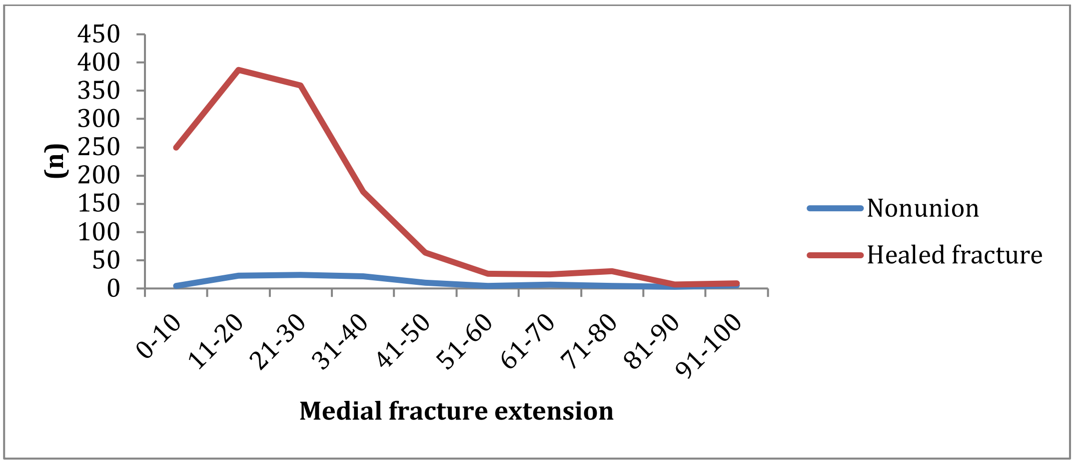


Figure 4-31 Frequency of nonunion according to length of medial cortex fracture extension.

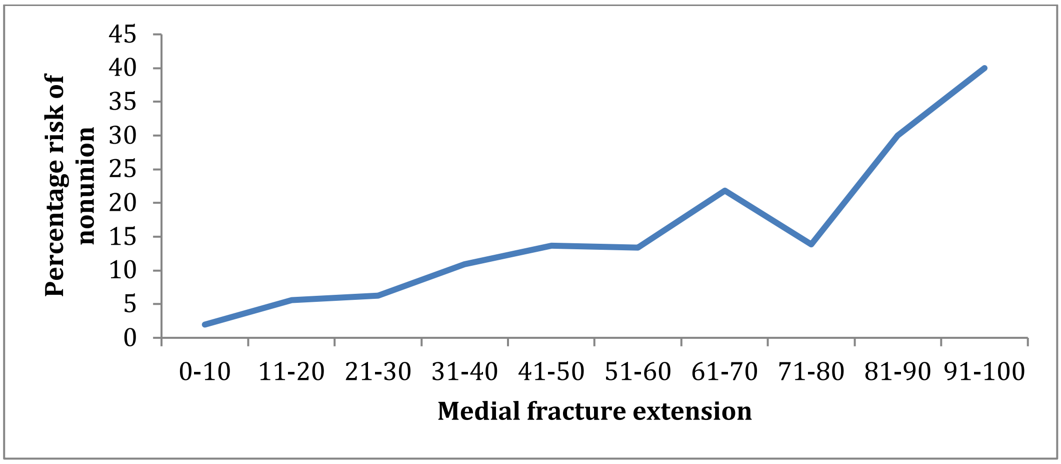


Figure 4-32 Percentage risk of nonunion according to length of medial cortex fracture extension.

Length of lateral cortex fracture extension

Fractures involving the humeral diaphysis were excluded from this section of the analysis. There was an approximately linear relationship between length of the lateral cortex fracture extension and the risk of nonunion. Increasing length of the lateral cortex fracture extension was associated with nonunion ($p < 0.001$, Bivariate binary logistic regression) (Figure 4-33) (Figure 4-34).

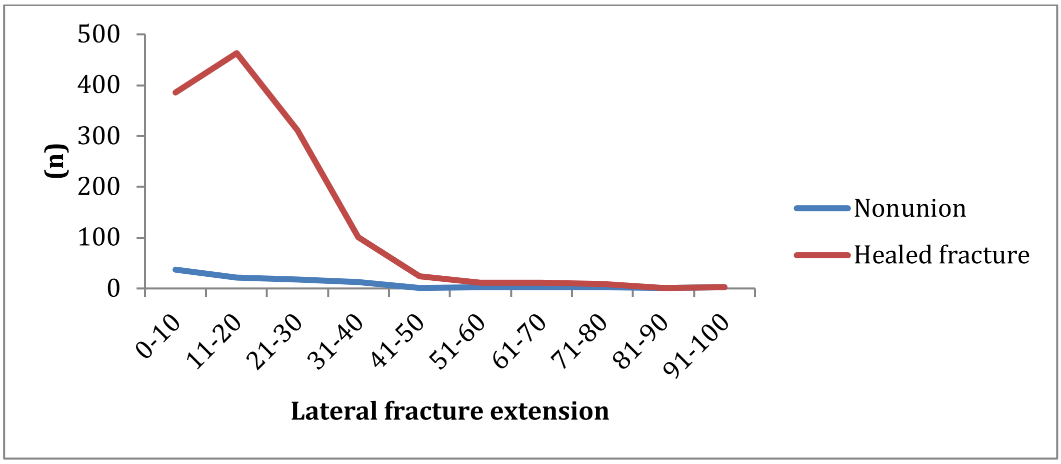


Figure 4-33 Frequency of nonunion according to length of lateral cortex fracture extension.

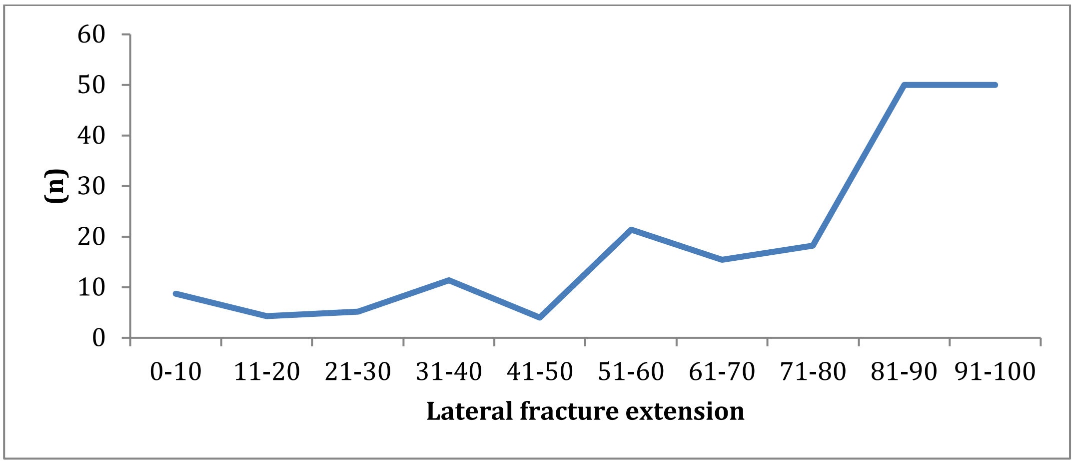


Figure 4-34 Percentage risk of nonunion according to length of lateral cortex fracture extension.

4.4.5 Multivariate analysis

All of the radiographic measurements predictive of nonunion on univariate analysis were included in the multivariate analysis. On multivariate analysis, only the continuous variables of humeral head angulation and humeral head-shaft translation and the categorical variables of tuberosity involvement and fracture separation remained independently predictive of nonunion. Examination of these variables revealed no significant interactions or multi-collinearity effects.

The regression coefficient B, odds ratio exp(B), and significance for each variable used for estimating the risk of non-union in the final model are depicted in Table 4-2.

Measurement	Regression coefficient (B)	Wald statistic	*p* value of Wald statistic	Standard error of B	Odds ratio Exp (B) (95% CI)
Head angle	-0.43	46.435	<0.001	0.006	0.958 (0.946 - 0.970)
Tuberosity involvement	-1.205	12.335	<0.001	0.343	0.300 (0.153 - 0.587)
Translation	0.034	90.647	<0.001	0.004	1.034 (1.027 - 1.042)
Separation	1.438	15.713	<0.001	0.363	4.212 (2.069 - 8.577)

Table 4-2 Logistic regression model for prediction of nonunion after NHF.

4.4.6 Predictive formula

The method of calculating the probability of non-union in an individual patient is as follows:

y = (-0.043 x humeral head angulation) + (-1.205 if tuberosity fracture) + (0.034 x humeral head-shaft translation) + (1.438 if separation) + 1.467. Probability nonunion (percentage) = 100[e^y] / [1 + e^y].

The four radiographic variables can be input into the above formula using a excel spreadsheet to produce a predicted probability of nonunion to guide clinicians. Table 4-3 shows probability of nonunion according to the predictive formula for various fracture patterns.

Head angle (°)	Tuberosity involvement	Translation (%)	Separation	Probability of nonunion (%)
130	No	0	No	1.59
130	No	25	No	3.65
130	No	50	No	8.14
130	No	100	No	32.67
130	Yes	0	No	0.48
130	Yes	25	No	1.12
130	Yes	50	No	2.59
130	Yes	100	No	12.70
90	No	0	No	8.29
90	No	25	No	17.47
90	No	50	No	33.11
90	No	100	No	73.05
150	Yes	0	No	0.20
150	Yes	50	No	0.48
130	No	25	Yes	13.67
130	No	50	Yes	27.19

Table 4-3 The probability of nonunion according to the predictive formula for various fracture patterns.

4.4.7 Evaluation of nonunion prediction formula

The Hosmer- Lemeshow chi-square value of the model was 14.227 on eight degrees of freedom (p = 0.076). The model, based on the four radiographic predictors, was therefore judged to be of high quality according to the Hosmer-Lemeshow goodness-of-fit statistic. The performance of the model according to decile risk of nonunion is shown in Table 4-4. The Wald chi-square statistic for each of the radiographic predictors achieved significance in the final model (Table 4-2).

Decile of risk	Number of patients	Number of nonunions	Observed %	Predicted %
1	202	0	0	0.16
2	180	2	1.11	0.37
3	160	0	0	0.77
4	171	0	0	1.19
5	180	0	0	1.5
6	180	1	0.56	2
7	180	6	3.33	2.88
8	180	11	6.11	4.89
9	180	26	14.44	10.85
10	189	82	43.39	44.42

Table 4-4 Contingency table for the Hosmer and Lemoshow test demonstrating the performance of the model according to decile risk of nonunion.

The union outcome was cross-tabulated against the outcome predicted by the model in a 2 x 2 table to estimate the model's accuracy as a diagnostic test. Positive predictive values (PPV) and negative predictive values (NPV) for different thresholds of predicted probability are depicted in Table 4-5. The sensitivity of the model is the proportion of nonunions correctly identified at a particular threshold value, whereas PPV is the proportion of patients with nonunion who are correctly diagnosed at a particular threshold. The specificity and NPV provide similar estimates for fracture union. Decreasing the threshold for diagnosis of nonunion from 50% increases the sensitivity of the model to detect a higher proportion of nonunions, but it decreases the PPV of the model at that particular threshold. In contrast, decreasing the threshold for diagnosis decreases the specificity of the model to predict union while increasing the NPV. The overall percentage of correct diagnoses is lower at lower threshold values than at higher thresholds.

If all NHF were managed operatively, the calculated NNT to prevent a single nonunion was 14.1. If only those fractures with a predicted nonunion probability of >= 40% were managed operatively, the NNT fell to 1.7. The area under the receiver operating characteristic curve was 0.92 (Figure 4-35).

Threshold probability of nonunion	"At Risk"* (%)	Positive Predictive Value (%)	Correct to Incorrect Diagnoses in Operative Group	Negative Predictive Value (%)	Surgical Procedures per Nonunion	Total Percentage Correct	Sensitivity	Specificity
100%, nonoperative treatment for all	0	No patients managed operatively	No patients managed operatively	92.9	No patients managed operatively	92.9	0	100
90%	0.33	80	5	93.15	1.2	93.12	3.91	99.94
80%	1.39	80	4	93.92	1.25	93.73	15.63	99.7
70%	1.89	79.41	3.86	94.29	1.26	94.01	21.09	99.58
60%	2.66	72.92	2.69	94.7	1.37	94.12	27.34	99.22
50%	3.27	64.41	1.81	94.84	1.55	93.84	26.69	98.75
40%	4.94	59.56	1.47	95.62	1.68	93.84	41.41	97.85
30%	6.6	53.78	1.16	96.2	1.86	93.4	50	96.71
20%	9.1	47.56	0.91	96.95	2.1	92.45	60.94	94.86
10%	15.87	33.92	0.49	97.95	2.96	87.74	75.78	88.65
5%	24.86	25.89	0.35	99.11	3.86	80.91	90.63	80.17
1%	71.7	9.75	0.11	99.67	10.25	35.18	98.44	30.35
0%, primary operative treatment for all	100	7.1	0.07	All patients managed operatively	14.08	7.1	100	0

Table 4-5 Performance of the multivariate model at different thresholds

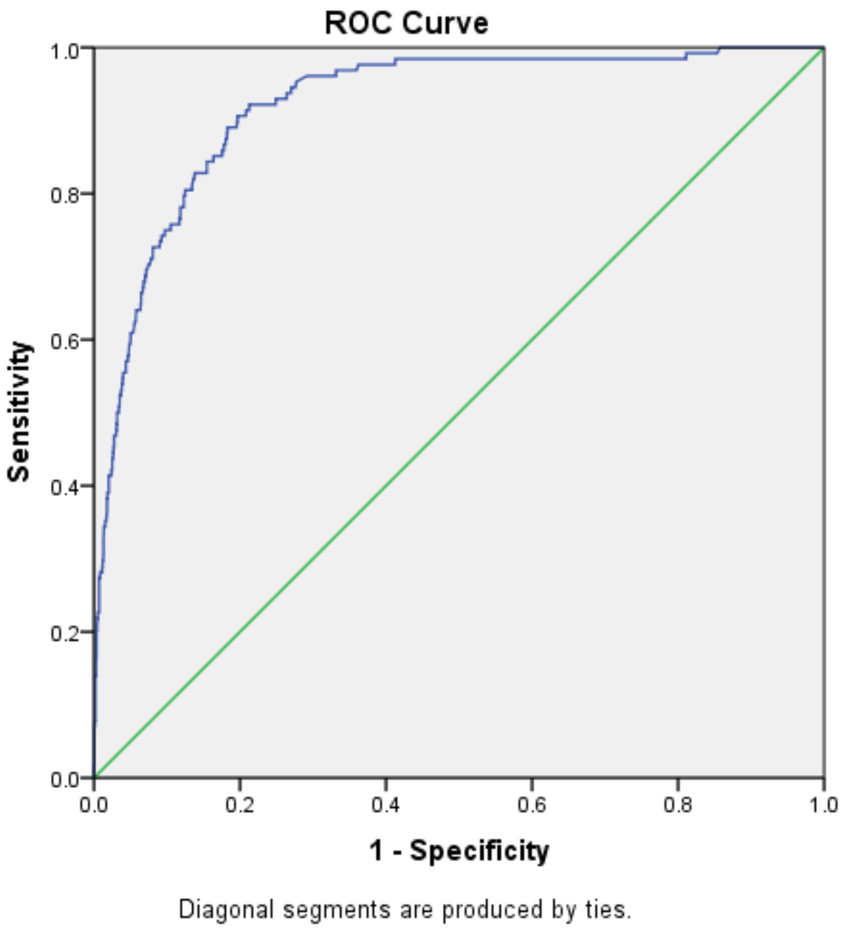


Figure 4-35 Receiver operating characteristic curve for the logistic regression model.

4.5 CHAPTER DISCUSSION

Nonunion occurred in 128 (7.1%) of patients who were at least 16 years of age. Although historical estimates of the rate of nonunion after NHF are varied, the results of this chapter support the prevalence reported in more contemporary studies(3, 79, 80). Worsening social deprivation was predictive of nonunion but increasing age, gender and mode of injury were not. Four radiographic factors were found to be independently predictive of nonunion on stepwise multiple logistic regression. They were increasing humeral head-shaft translation, increasing varus angulation of the humeral head, separation at the fracture site and absence of an associated tuberosity fracture. The risk of nonunion in a completely undisplaced fracture was close to zero but this increased to an appreciable value with more complex fracture patterns and displacements. Using a multivariate model that takes the four identified radiological risk factors into account, estimates of risk of nonunion after nonoperative management can be produced.

There is limited literature evaluating the effect of patient factors upon nonunion after NHF. This is the first study demonstrating the detrimental effect of worsening social deprivation on healing after NHF. Increasing age was not predictive of nonunion and this is in keeping with the results of a previous large population based study which found a higher rate of nonunion in young and middle-aged adults rather than in the older and elderly population (80). Factors associated with socioeconomic status that may influence fracture healing are smoking, alcohol, nutrition and other medical comorbidities (114, 115). These factors were not specifically recorded in this study so it was not possible to evaluate their individual roles. Other specific factors that that might increase the risk of nonunion but were not measured include rheumatoid disease, immunocompromised, renal failure, epilepsy and use of drugs such as corticosteroids and those interfering with vitamin-D metabolism. CHAPTER 7 investigates the relationship between patient factors and nonunion in more detail.

The results of this chapter confirm the importance of NHF pattern on healing. Increasing translation of the humeral head in relation to the shaft increases the risk of nonunion. This probably reflects the severity of underlying osseous and soft tissue injuries. Severe displacement and disruption of the periosteal sleeve causes instability between the humeral head and shaft, and can result soft tissue interposition of periosteum, muscle, and the tendinous portion of the long head of biceps, inhibiting callus formation. Worsening varus angulation of the humeral head was associated with and increased risk of nonunion. As the head angle decreases the bony apposition between the head and shaft decreases and this is most notable when the angulation is less than 90 degrees. Due to the pull of the rotator cuff and the lack of bony apposition, fractures that have an initial head angulation of less than 90 degrees tend to displace into further varus over time which again makes these fractures less likely to heal. Separation at the fracture site was independently predicative of nonunion, again probably due to the consequences of soft tissue interposition. Absence of tuberosity fracture was independently predictive of nonunion. It may be that in these fractures, the intact rotator cuff and its resultant muscle pull predispose to nonunion by causing secondary displacement of the head in relation to the shaft over time.

One previous study by Hertel found a short intact medial calcar to be associated with intraoperative humeral head ischaemia(50). Despite this finding, a follow-up study from the same authors found a poor correlation between intraoperative ischaemia and the development of avascular necrosis(55). This discrepancy is supported by a more recent study in which tetracycline was administered to patients prior to undergoing hemiarthroplasty for proximal humerus fractures. Humeral head specimens were obtained from the surgery and analysed sing fluoroscopic microscopy. Fluorescence was observed in all specimens suggesting that vascular supply was not disrupted in any of the fracture patterns(56). The results of the present study also contradict Hertel's initial study findings as an increased length intact medial calcar was associated with nonunion on univariate but not multivariate analysis. In the present study it is likely that length on intact medial calcar was a confounding variable that was present in fracture with other features that put it at high risk of nonunion rather than it being a cause of nonunion itself. Indeed, many subtuberosity fractures in which separation is a predisposing factor for nonunion also have a long intact medial calcar.

There were no standardised methods in the literature for many of the radiographic measurements that were made in section 4.3.1 and new techniques for these measurements therefore had to be adopted. In particular, measurement of the humeral head angulation was given careful consideration as it is possible to either measure the angle of the humeral head in relation to the humeral shaft or the glenoid. For the majority of minimally displaced fractures the angle between the humeral head and the humeral shaft and the humeral head and the glenoid are similar, as the AP radiograph is taken with the arm in a position in which the humeral shaft is approximately parallel to longitudinal axis of the glenoid. However, measuring the angle between the humeral head and shaft is less satisfactory in fractures with complex three-dimensional displacements especially where there is significant translation and angulation of the humeral shaft. Using the glenoid as the reference point in these injuries more accurately reflects the angular deformity of the humeral head. Additionally, measuring the angle between the humeral head and glenoid is straightforward and reproducible in all fractures, even in the presence of complex shaft displacements.

This study has a number of weaknesses. 274 (10.7%) patients underwent primary operative treatment before 3 months and were therefore excluded from the analysis. Primary operative treatment was offered at the discretion of the individual surgeon and it is almost certain that some of these patients would have been at high risk of nonunion. If all of these fractures were treated nonoperatively and had healed the overall rate of nonunion would have been 6.2%. On the other hand, if they had all failed to heal, the overall rate of nonunion would have been 19.3%.

This retrospective nature of the study design meant that a large sample size could be investigated which was essential as nonunion after NHF is rare. However, there are a number of limitations associated with this type of study design. Firstly, 441 patients (17.3%) had radiographs that were inadequate to make the measurements described in section 4.3.1 and these patients had to be excluded from the study. Due to the complex three-dimensional configurations of NHF, high quality, anteroposterior and modified axial radiographs are required to accurately make measurements of displacement, translation and angulation. Subtle inconsistencies in patient positioning and radiographic projection make standardisation challenging. Three-dimensional computed tomography might improve the reproducibility of measurements in more complex fractures but during the study period its use was limited by cost and higher radiation dosages.

Diagnosing the primary outcome measure of nonunion by retrospective review of case notes and fracture radiographs was another study limitation. Whilst defined criteria, described in section 2.4.2, were used to diagnosed nonunion there is the potential for misclassification bias. Although radiography allows a qualitative assessment of callus formation and cortical bridging, doubt has been cast over its reliability for the assessment of fracture healing and there is currently no accepted standardized definition of fracture nonunion among orthopaedic surgeons (117). Radiographic scoring systems have been developed for the hip (RUSH score) and the tibia (RUST score) however no such score exists for NHF (118, 119). The RUSH score is based on trabeculation across the fracture and similar concept was used to define nonunion in the present study. Computed tomography is increasingly being used to help make the diagnosis of nonunion and there is evidence that this imaging modality might have some advantages over plain radiographs. One study reported computed tomography to have 100% sensitivity for detecting nonunion in tibial fractures; however, it was limited by a low specificity of 62%(120). Cost and radiation dose of computed tomography scans limit its widespread use and indeed it was not routinely as an assessment tool for fractures healing during the study period. There is evidence that ultrasound is able to detect callus formation before radiographic changes are visible. One study showed that ultrasound findings at six and nine weeks had a 97% positive predictive value and 100% sensitivity in determining fracture healing in patients with acute tibial fractures treated with intramedullary nailing. Time to determination of healing was also shorter using ultrasound (6.5 weeks) compared to nineteen-week average of radiographic data. Ultrasound has additional advantages over other imaging modalities including lower cost, no ionizing radiation exposure, and being non-invasive. However, its use and interpretation of findings are thought to be highly dependent on operator's expertise and was not part of routine clinical care during the present study.

The statistical model allows estimation of the risk of nonunion in patients with NHF undergoing nonoperative management. However, because of the low probability of nonunion, the ability for the model to accurately predict nonunion in individual patients is limited. Although it is possible to select a particular threshold of estimated risk below which we can be fairly certain that patients will not develop nonunion, it is less certain that patients above the threshold will develop this complication. This is a common problem with statistical models that evaluate outcomes of low prevalence. Lowering the threshold for the predicated probability increases the sensitivity of the model to identify those who will develop nonunion, but at the expense of reducing the overall accuracy of the model to correctly identify those who will heal and reducing the overall percentage of correct diagnoses.

The predicted probability of nonunion should be used to guide clinicians in counselling patients rather than to apply an arbitrary threshold of risk to determine the management strategy. Furthermore, the ability of the model to predict a higher risk of nonunion in certain patients does not imply their outcome would be improved by primary operative intervention. By providing estimates of the probability of nonunion, it might be possible to raise awareness of the which patients are at highest risk of nonunion whilst minimising the number of patients undergoing unnecessary surgery. A limitation of the nonunion prediction formula is that four radiographic measurements have to be made and the slightly labour-intensive nature of this might be a barrier to uptake in a busy clinical environment. However, the majority of NHF are minimally displaced and the probability of nonunion following these injuries is low. A more focussed approach where clinicians might selectively apply the formula to the more complex fracture displacements is envisaged.

Following on from this study, a novel fracture classification based around radiographic predictors of nonunion is described in CHAPTER 5 and evaluated in CHAPTER 6 and CHAPTER 7.

CHAPTER 5
FRACTURE CLASSIFICATION

5.1 CHAPTER AIMS

This chapter aims to describe a novel classification for NHF.

5.2 INTRODUCTION

Despite its widespread use, the Neer classification has several shortcomings. Advances in imaging technology have permitted a better understanding of pathoanatomic factors that may be associated with prognosis which are not accounted for in the Neer classification and intraobserver and interobserver reliability are only fair to moderate. A full review of the fracture classification literature is presented in CHAPTER 1. Only when an adequate classification system is available will surgeons be able to collaborate to produce well-designed comparative clinical outcome studies, to enable proper evidence-based management of these injuries. An ideal fracture classification should be comprehensive - providing a means of describing all of the commonly encountered, clinically relevant fracture patterns, be based on a standard, easily obtained radiographic series, have an acceptable level of inter- and intra- observer reliability and importantly be of use in predicting outcome of different fracture types. A novel fracture classification had been designed in an attempt to satisfy these requirements. The development process and classification is described in sections 5.3 and 5.4.

5.3 DEVELOPMENT OF THE NOVEL FRACTURE CLASSIFICATION

The classification was developed by the author (EBG) an orthopaedic research fellow and CMR, a consultant orthopaedic surgeon with the intention that it would be suitable for use in every day clinical practice. It was agreed that the classification should satisfy the following criteria:

1. The fracture classification should be based on plain radiographs.
2. There should be a small number of broad groups that are based on commonly encountered fracture patterns.
3. Within each broad group there should be subgroups that are related to outcome
4. Each broad group and subgroup within it should be clearly defined using objective radiographic criteria.

5.3.1 **The fracture classification should be based on plain radiographs**

A fracture classification must be based on a readily available imaging modality if it is to be widely adopted for routine clinical use. In current clinical practice, only a minority of patients with more complex fractures undergo CT scanning and there is no agreed protocol for which fractures should undergo CT scanning either within or between institutions. It was therefore decided that the fracture classification should be based on plain radiographs and it should be possible to assign a fracture to any subgroup in the classification without the need for CT scanning.

5.3.2 There should be broad groups that are based on commonly encountered fracture patterns

From review of the literature, three well established, commonly encountered fracture patterns were identified. These were ‘undisplaced’ fractures, ‘medial impaction’ (varus) fractures and ‘lateral impaction’ (valgus) fractures. EBG and CMR attempted to group each fracture from database 1 into these three patterns. During this process an additional two patterns which had not been previously described were frequently encountered. These were termed ‘early medial separation’ fractures and ‘subtuberosity’ fractures. The final classification was based around these five broad groups of commonly encountered fracture patterns.

Early medial separation fractures

Early medial separation fractures share a similar mechanism of injury to valgus fractures where the predominant force is lateral compression, however the resulting initial deformity differs. In valgus fractures, the lateral cortex fails early, leading to valgus collapse of the humeral head and splaying of the tuberosities. The medial hinge remains intact in the majority valgus fractures and medial translation of the shaft only occurs after extreme collapse of the head in more severe injuries. In contrast to this, in early medial separation fractures, the medial hinge fails early resulting in early medial translation of the humeral shaft without the significant preceding valgus collapse of the humeral head.

Subtuberosity fractures

The mode of failure in these fractures is torsional or bending forces rather than compression. The principal fracture line occurs below the level of the surgical neck and is centred in the distal third of the modified Mullers box.

5.3.3 **Within each broad group there should be subgroups that are related to outcome**

A fracture classification should be of use in predicting outcome. Each broad group was therefore divided into smaller subgroups based on the severity of the fracture. In order to do this, determinants of fracture severity had to be identified. A review of the NHF literature was performed and is presented in CHAPTER 1.

From the literature it is apparent that poor outcome following NHF is usually due to the development of a complication. The three important potential complications are nonunion between the humeral head and shaft, malunion of the tuberosities leading to rotator cuff dysfunction and osteonecrosis of the humeral head.

The next decision was which of these three complications to base the classification on. Nonunion is straightforward to diagnose clinically and results in significant shoulder disability and therefore it was decided that the classification should be designed around this. In patients with healed fractures, rotator cuff dysfunction is a major determinant of poor functional outcome and so the decision was made to include this too. Osteonecrosis represents a spectrum of presentation and there is a lack of precise radiological guidelines for its assessment which make diagnosis difficult. For this reason, osteonecrosis was not an important concept of the fracture classification.

Having decided to base the novel classification on nonunion and rotator cuff dysfunction, the next step was to identify radiographic factors related to these two complications.

The study presented in CHAPTER 4 identified four radiographic predictors of nonunion. These were increasing translation of the humeral head in relation to the shaft (head-shaft translation), increasing varus angulation of the humeral head (head angulation), separation at the fracture site and absence of associated tuberosity fracture.

On this basis, the concept of classifying fractures according to 'stability' was introduced. An 'unstable' fracture was one with radiographic features which might predispose it to nonunion. Conversely, a 'stable' fracture was one without these. A decision had to be made regarding which of the four radiographic predictors identified in CHAPTER 4 to include in the classification as features of 'instability'. The decision was made to include head-shaft translation, head angulation and separation.

Head-shaft translation and head angulation are continuous variables and therefore a cut point had to be introduced so that fractures could be described as stable or unstable in relation to them. The cut point for head-shaft translation was set at 50% and the cut point for head angulation was set as 90 degrees. These cut points were chose for two reasons. Firstly, fractures on either side of each cut point can easily be identified on plain radiographs, and secondly, the risk of nonunion increases substantially in fractures with greater than 50% head-shaft translation and also in fractures with less than 90 degrees of head angulation as shown in Figure 4-20 and Figure 4-26. Separation was a binary variable and any fracture with separation present was considered unstable.

The decision was made to involve the presence or absence of an associated displaced tuberosity fracture in the classification. Rather than its implication in predicting nonunion, displacement of the tuberosities was included as it is well recognised that malunion is associated with poor functional outcome. A tuberosity was considered displaced when the displacement was ≥1mm.

Initially four fracture categories were developed based on combining the principles of fracture 'stability' and displacement of the tuberosities. The four categories were as follows:

1. 'Stable' fracture without a displaced tuberosity fragment.
2. 'Stable' fracture with a displaced tuberosity fragment.
3. 'Unstable' fracture without a displaced tuberosity fragment.
4. 'Unstable' fracture with a displaced tuberosity fragment.

5.3.4 Each broad group and subgroup within it should be clearly defined using objective radiographic criteria

A fracture classification should have an acceptable level of inter- and intra- observer reliability. In order to achieve this, it was decided that for a fracture to be assigned to a broad group or a subgroup within it there must be a clearly defined, objective set of criteria that it must meet. This should make the classification more user friendly and allow users who are relatively unfamiliar with the classification to correctly classify a fracture.

5.3.5 **Finalising the novel fracture classification**

The risk factors for poor outcome described in section 5.3.3 were used to define different subgroups within each clinically relevant pattern. The subgroups were largely based on ‘stability’, and the involvement of an associated displaced tuberosity fracture

Each subgroup was assigned a set of defining radiographic features that had to be fulfilled for a fracture to be placed within it. Illustrations of fractures were made with the key features highlighted and this was supplemented with radiographic examples. The fracture classification subgroups and the criteria for inclusion are described in detail in section 5.4.

5.4 RESULTS

The fracture classification is described in this section. The criteria for inclusion in each group is described, alongside example illustrations and radiographs.

5.4.1 **UNDISPLACED FRACTURES (UD)**

Undisplaced fractures may present in either the anatomic neck, surgical neck or the subtuberosity region. In order for a fracture to be classified as undisplaced it must fulfil the following criteria:

1. There must be no impaction between the humeral head and shaft (<1mm).
2. There must be no separation between the humeral shaft and head.
3. The humeral head angulation must be neutral (between 130 and 140 degrees).
4. There must be no translation of the humeral shaft in relation to the head (<1mm).
5. There must be no associated tuberosity fracture.

Example illustrations and radiographs of this fracture are shown in Figure 5-1 and Figure 5-2.

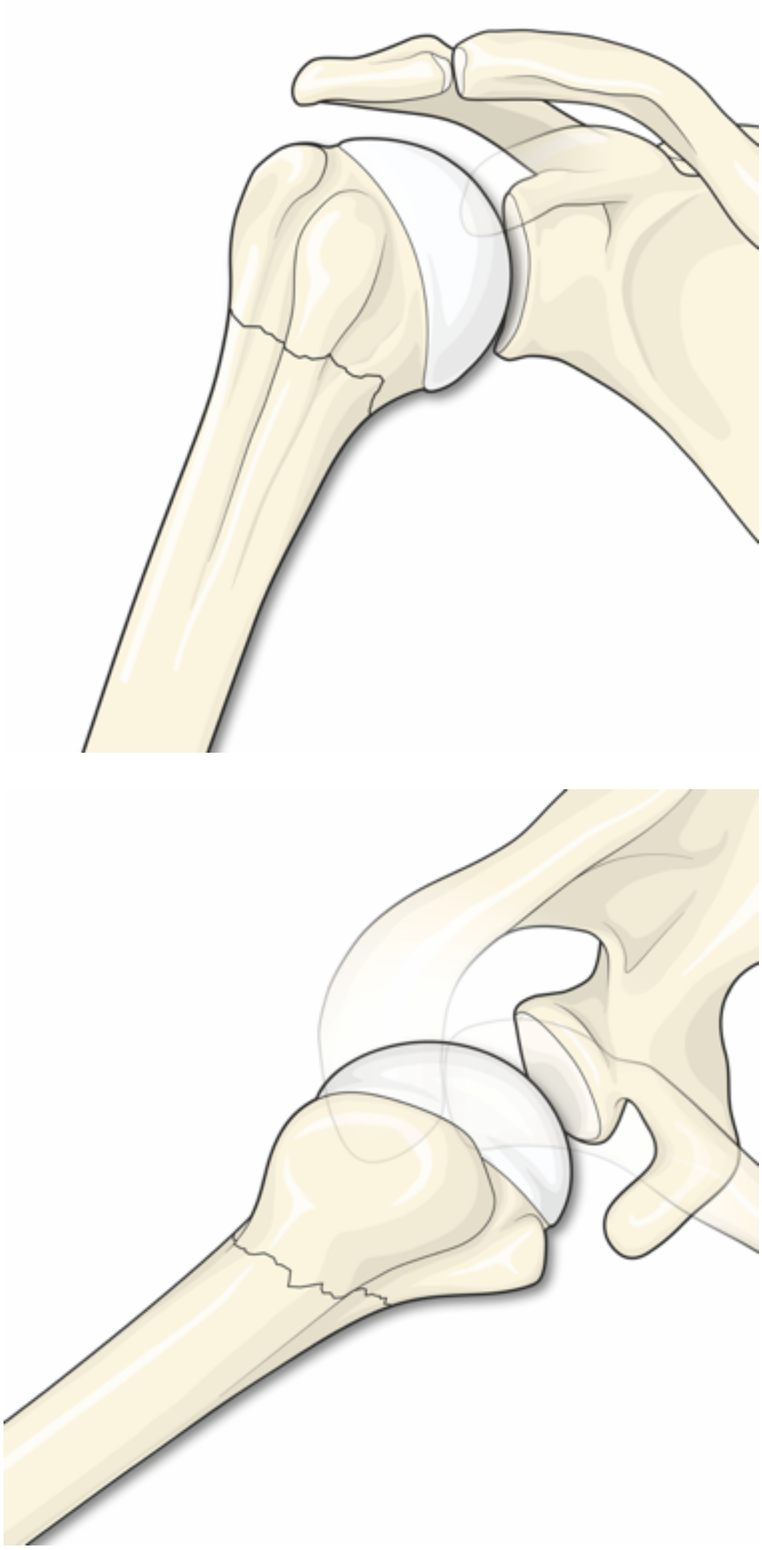


Figure 5-1 AP and modified axial illustrations of an undisplaced fracture.

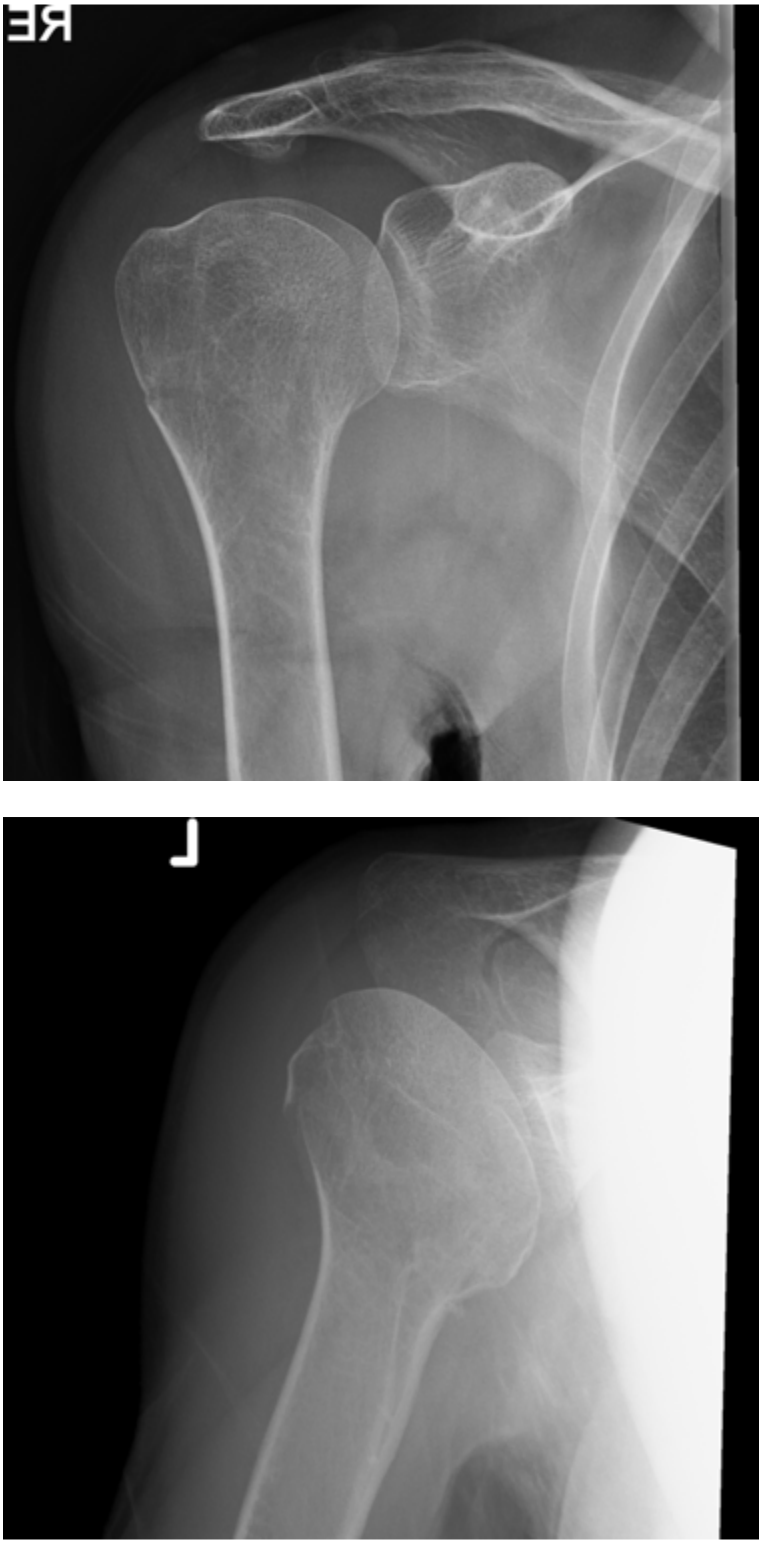


Figure 5-2 AP and modified axial radiographs of an undisplaced fracture.

5.4.2 **LATERAL COMPRESSION FRACTURES**

Lateral compression fractures are recognised by valgus orientation of the humeral head. When falling onto the outstretched and with the shoulder in flexion, abduction and internal rotation the glenoid forces the humeral head into valgus, hinging around the inferomedial aspect of the stronger calcar bone(25). The fracture exits medially at the level of the anatomical neck, leaving the calcar attached to the humeral shaft. Laterally, the head is driven into the proximal metaphysis of the shaft by axial loading, producing secondary tuberosity fractures. A fracture of the greater tuberosity is the hallmark of a lateral compression fracture as the humeral head cannot collapse into valgus without fracture and lateralisation of the greater tuberosity. Lateral impaction fractures represent a spectrum of injury, the severity of which is probably determined by the bone quality, arm position at the time of injury and the degree of energy transfer. The following characteristics must be present for a fracture to be placed in the lateral compression category:

1. There must be a fracture of the greater tuberosity.
2. The medial calcar is fractured from the head and is either attached to the shaft segment or may be comminuted.
3. The shaft is not driven superiorly and therefore gives the appearance of an intact gothic arch.
4. The principal neck fracture line is seen on the AP radiograph running through the anatomical neck.

5.4.3 Lateral compression 1 (LC1)

In these fractures, the deforming force transferred to the proximal humerus is relatively minor and there is an undisplaced fracture of the anatomical neck with a secondary fracture of the greater (and, also, rarely of the lesser tuberosity). The tuberosity fracture is usually the most striking feature on the radiographs. On the AP radiograph, the normal smoothly curved contour between the superior greater tuberosity and the lateral articular surface of the humeral head is intact. Whilst the humeral neck fracture can be subtle, with a high index of suspicion, it can usually be seen on conventional radiographs. Example illustrations and radiographs of this fracture are shown in Figure 5-3 and Figure 5-4.

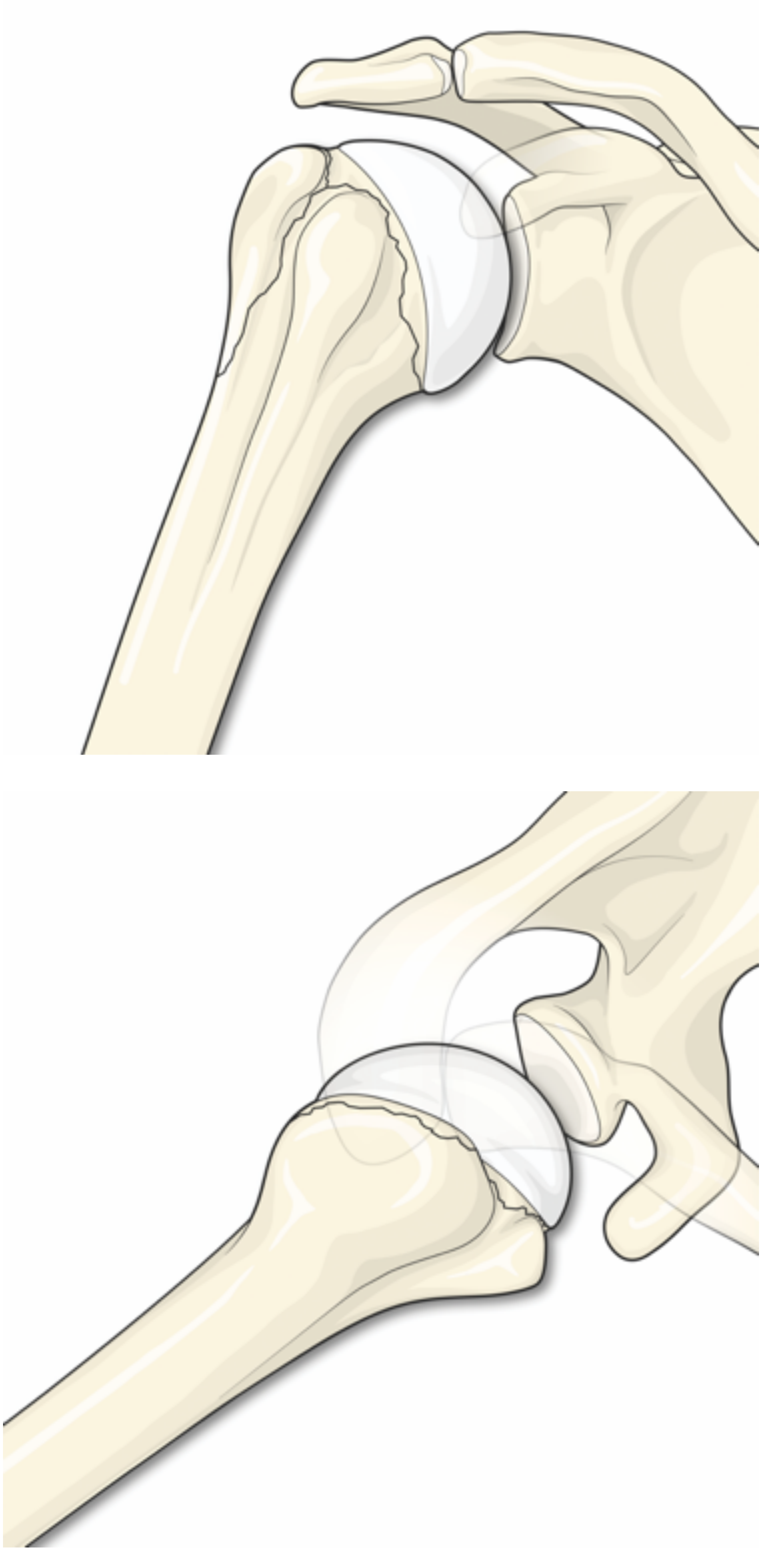


Figure 5-3 AP and modified axial illustrations of an LC1 fracture.

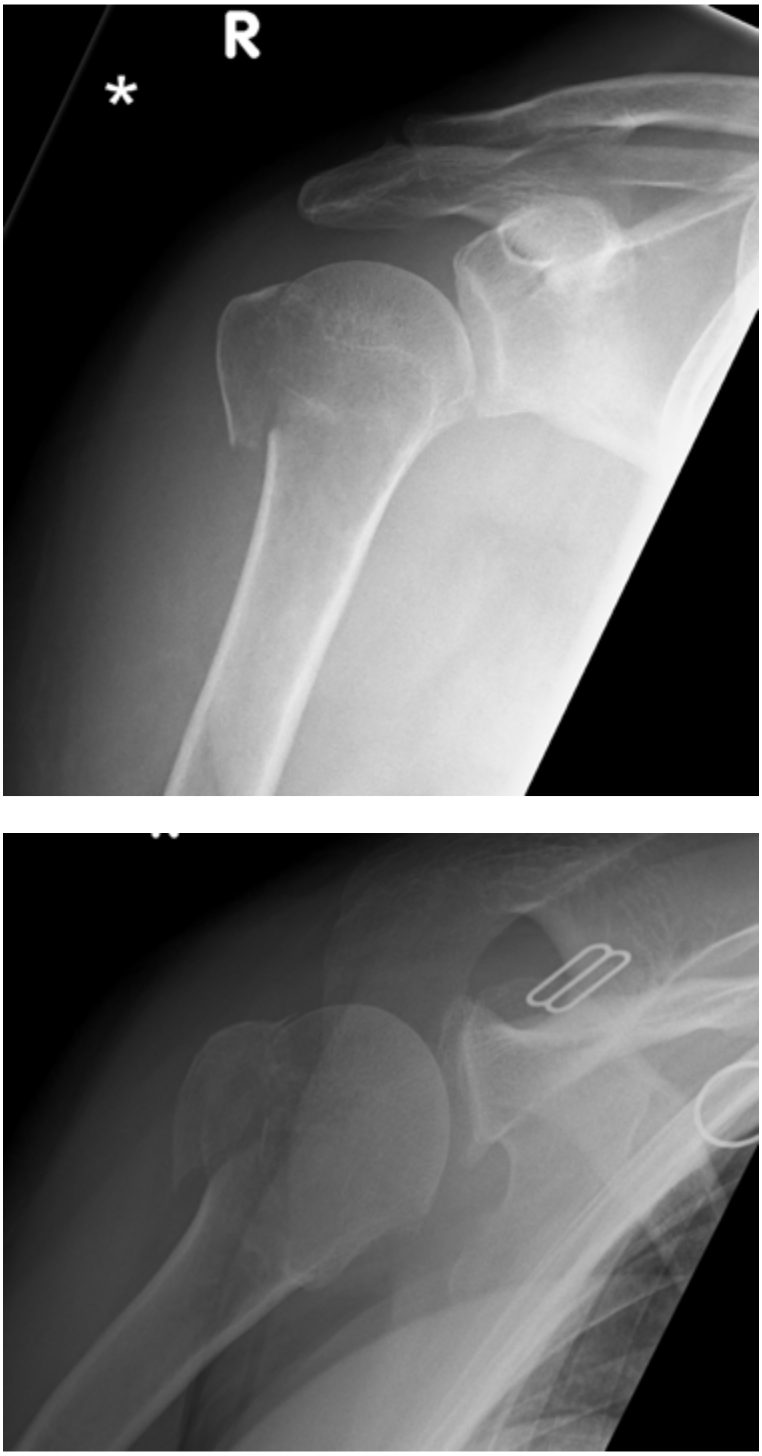


Figure 5-4 AP and modified axial radiographs of an LC1 fracture.

5.4.4 **Lateral compression 2 (LC2)**

When a greater axial loading force is applied, or if the proximal humerus is more osteoporotic, the humeral head is pushed into the metaphysis causing increasing amounts of valgus impaction(25). The intact periosteal hinge between the humeral head and the medial calcar is the axis around which the humeral head pivots as it is displaced. Both of the peripherally positioned tuberosities are pushed laterally and fractured by the incursion of the humeral head into the metaphysis. On the AP radiograph, the normal smoothly curved contour between the superior greater tuberosity and the lateral articular surface of the humeral head is lost as the head fragment collapses inferior to the greater tuberosity. Example illustrations and radiographs of this fracture are shown in Figure 5-5 and Figure 5-6.

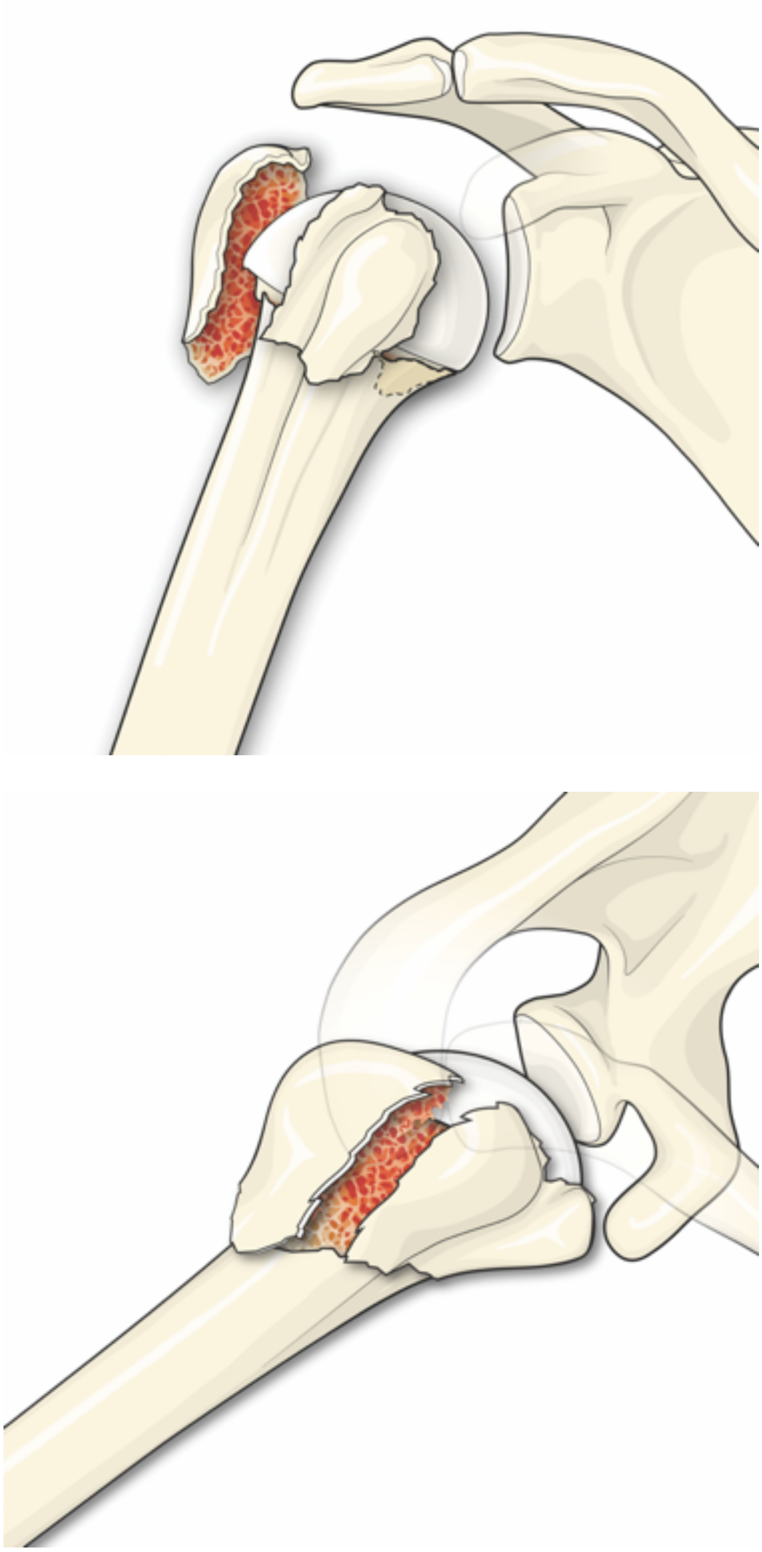


Figure 5-5 AP and modified axial illustrations of an LC2 fracture.

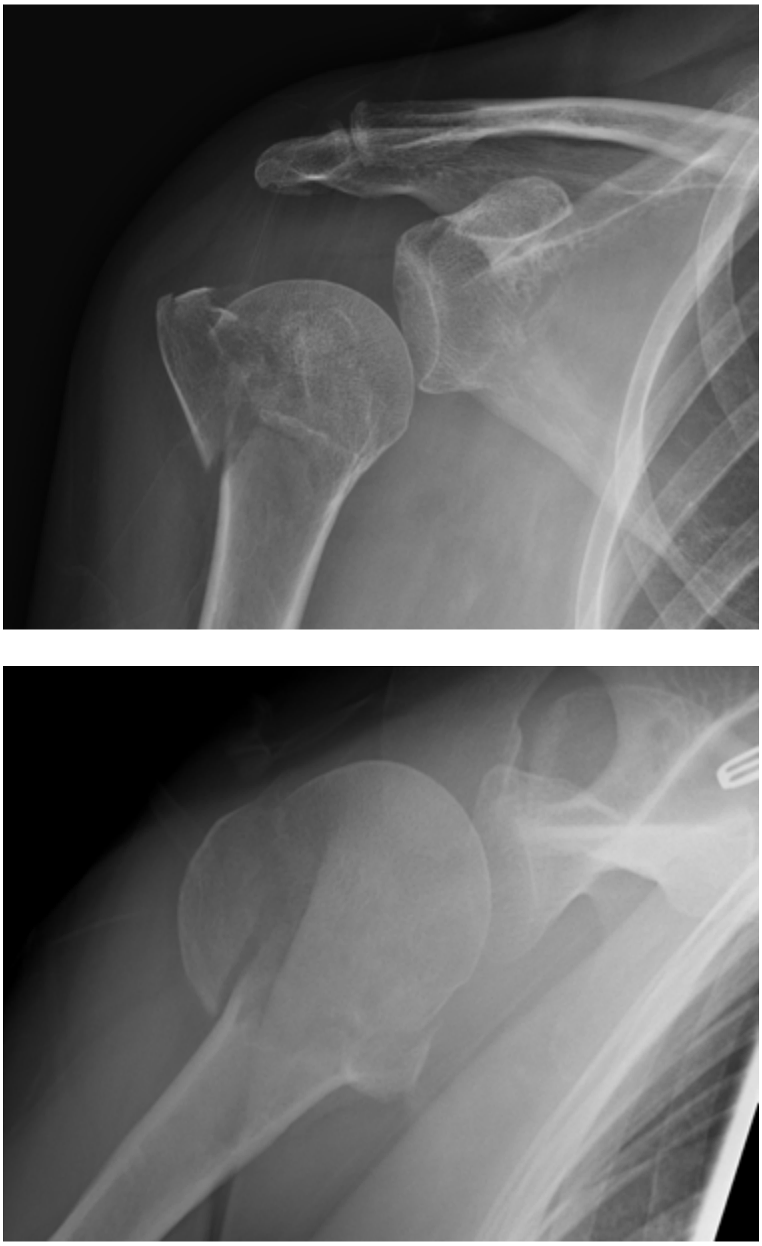


Figure 5-6 AP and modified axial radiographs of an LC2 fracture.

5.4.5 Lateral compression 3 (LC3)

In these fractures, the sharp medial calcar is exposed and the medial periosteal hinge begins to tear as it is stretched over the unyielding edge of the calcar. This results in medial displacement of the shaft relative to the calcar. Progression of the shearing of the capsule by the exposed medial calcar may progress such that the shaft becomes completely separated from the valgus angulated head which remains enlocated in the glenohumeral joint however this pattern of injury is uncommon and the vast majority of these fractures are stable injuries. Example illustrations and radiographs of this fracture are shown in Figure 5-7 and Figure 5-8.

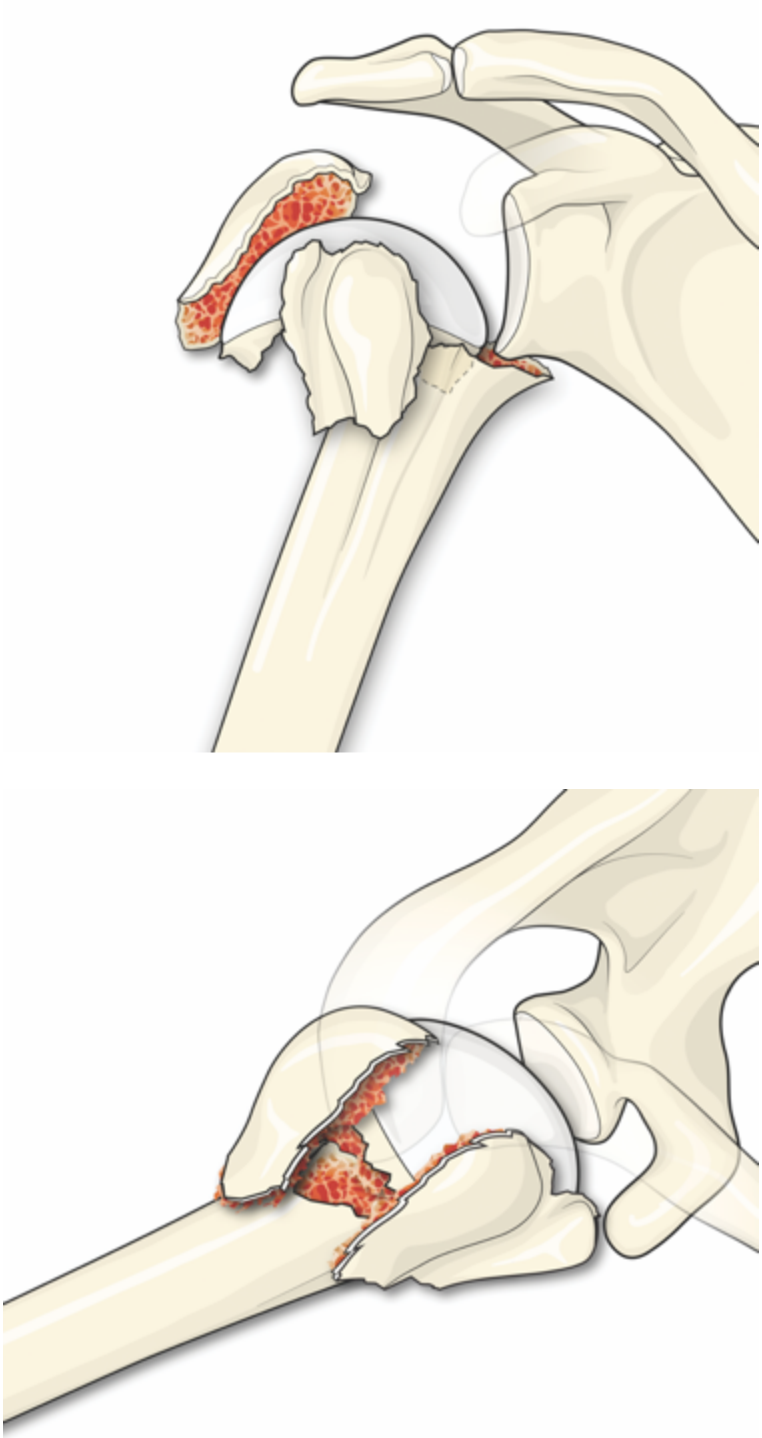


Figure 5-7 AP and modified axial illustrations of an LC3 fracture.

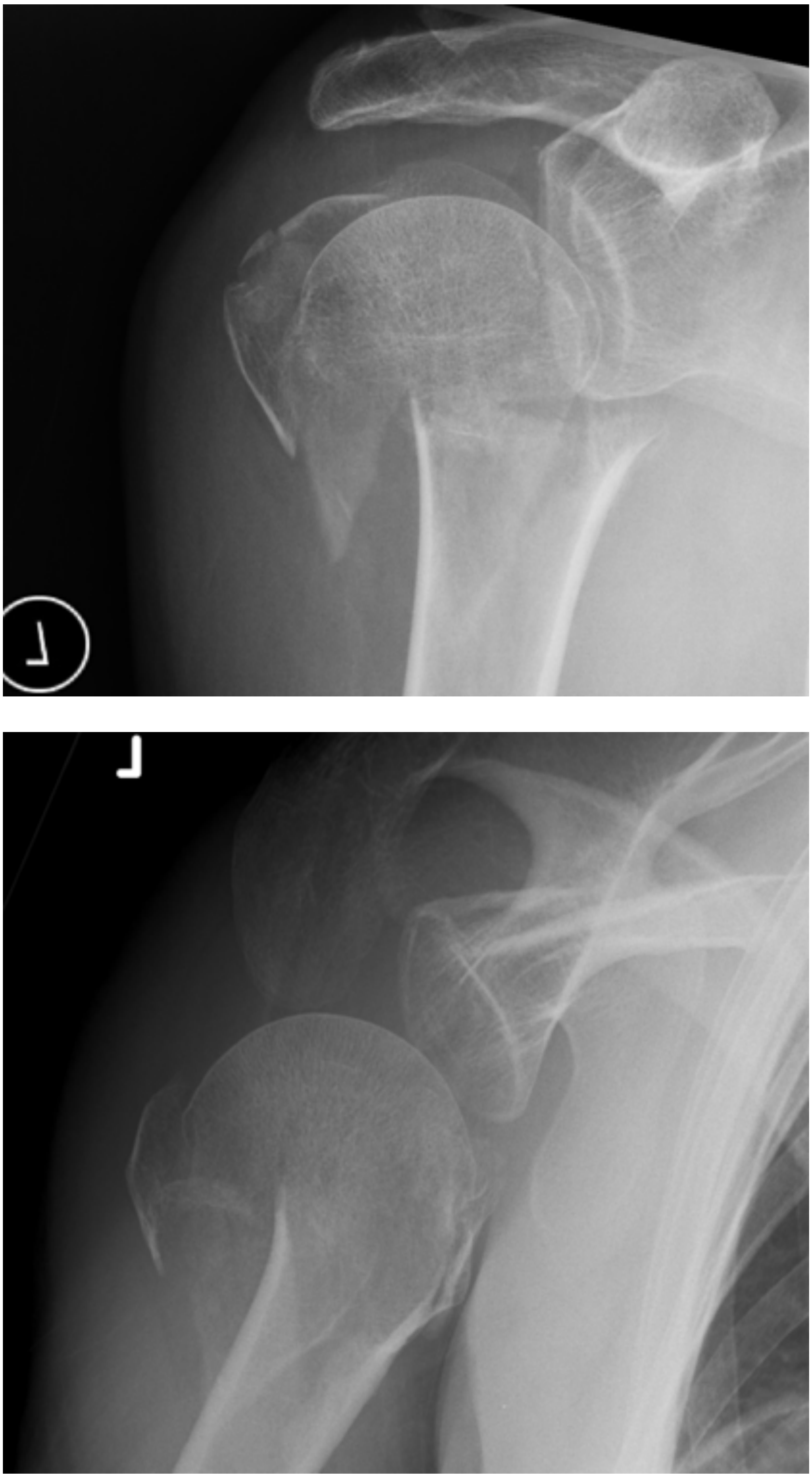


Figure 5-8 AP and modified axial radiographs of an LC3 fracture.

EARLY MEDIAL SEPARATION FRACTURES

The mechanism of injury in early medial separation fractures is lateral compression, however the medial hinge fails before the lateral cortex. This results in medial translation of the humeral shaft without valgus angulation of the humeral head. There may or may not be an associated tuberosity fracture.

5.4.6 **Early medial separation 1 (EMS1)**

The fracture occurs at the anatomical neck. There is medial translation of the shaft in relation to the head but under 50%. There is not excessive varus or valgus angulation of the humeral head. There may or may not be an associated tuberosity fracture. Example illustrations and radiographs of this fracture are shown in Figure 5-9 and Figure 5-10.

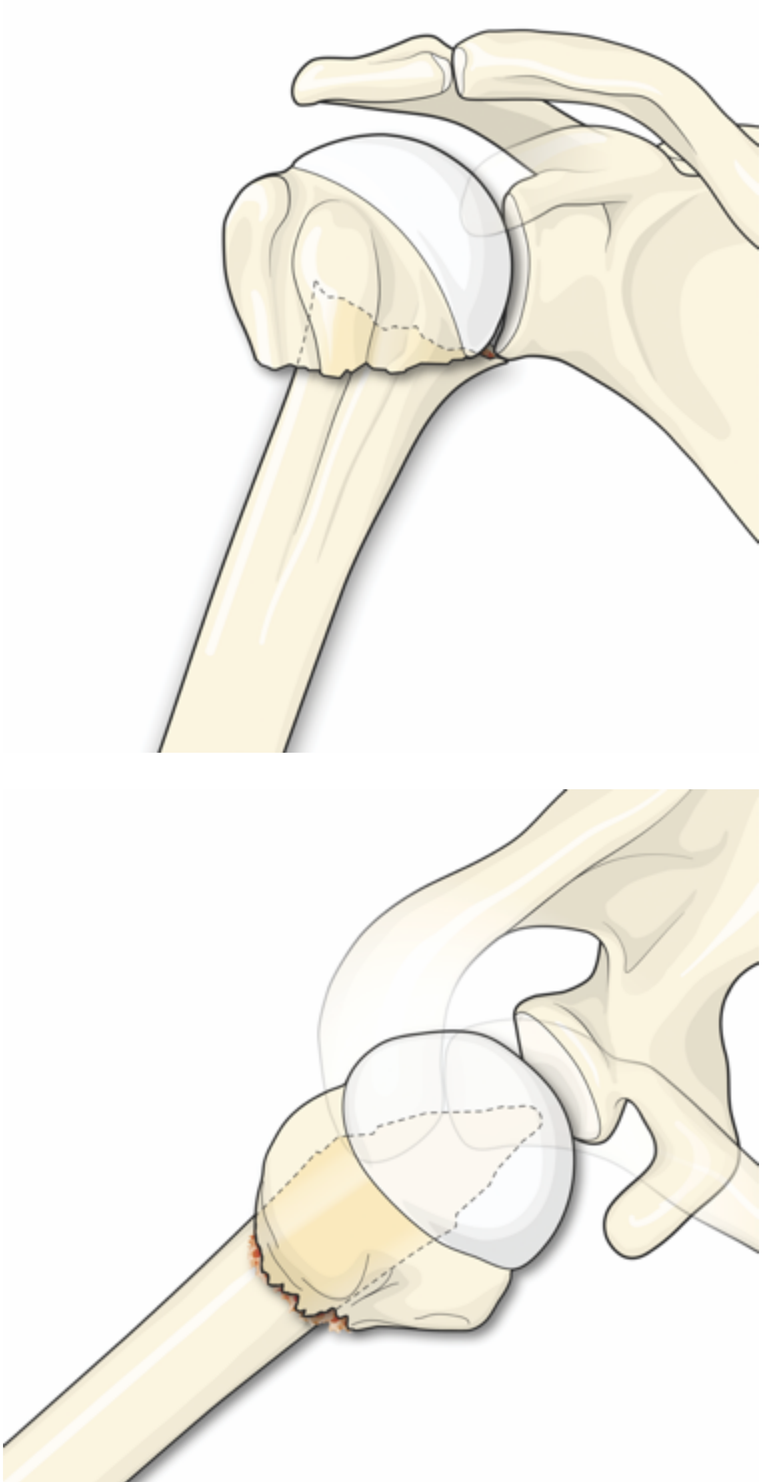


Figure 5-9 AP and modified axial illustrations of an EMS1 fracture.

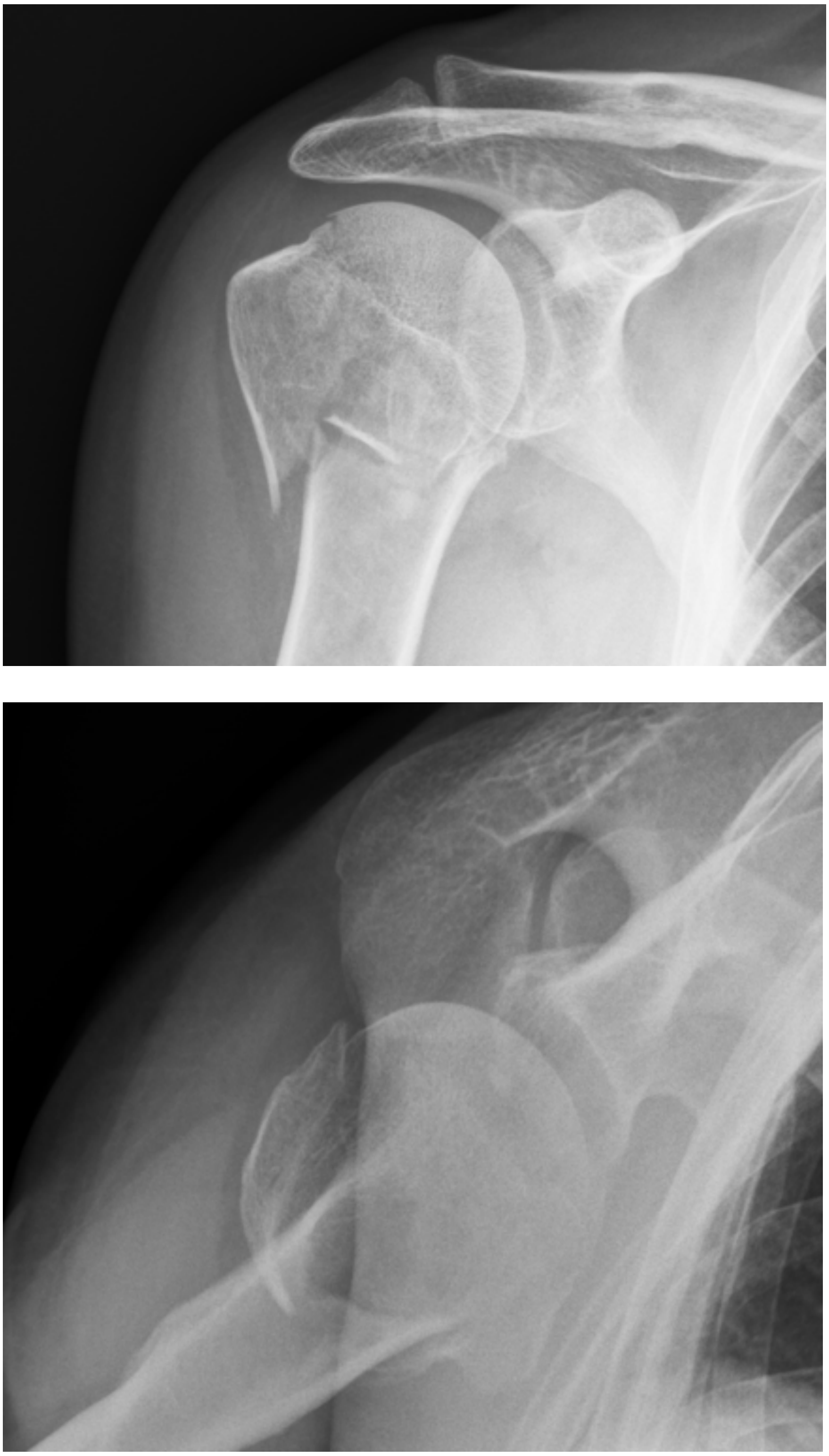


Figure 5-10 AP and modified axial radiographs of an EMS1 fracture.

5.4.7 **Early medial separation 2 (EMS2)**

The fracture occurs at the anatomical neck. There is medial translation of the shaft in relation (over 50%). There is not excessive varus or valgus angulation of the humeral head. There may or may not be an associated tuberosity fracture. Example illustrations and radiographs of this fracture are shown in Figure 5-11 and Figure 5-12.

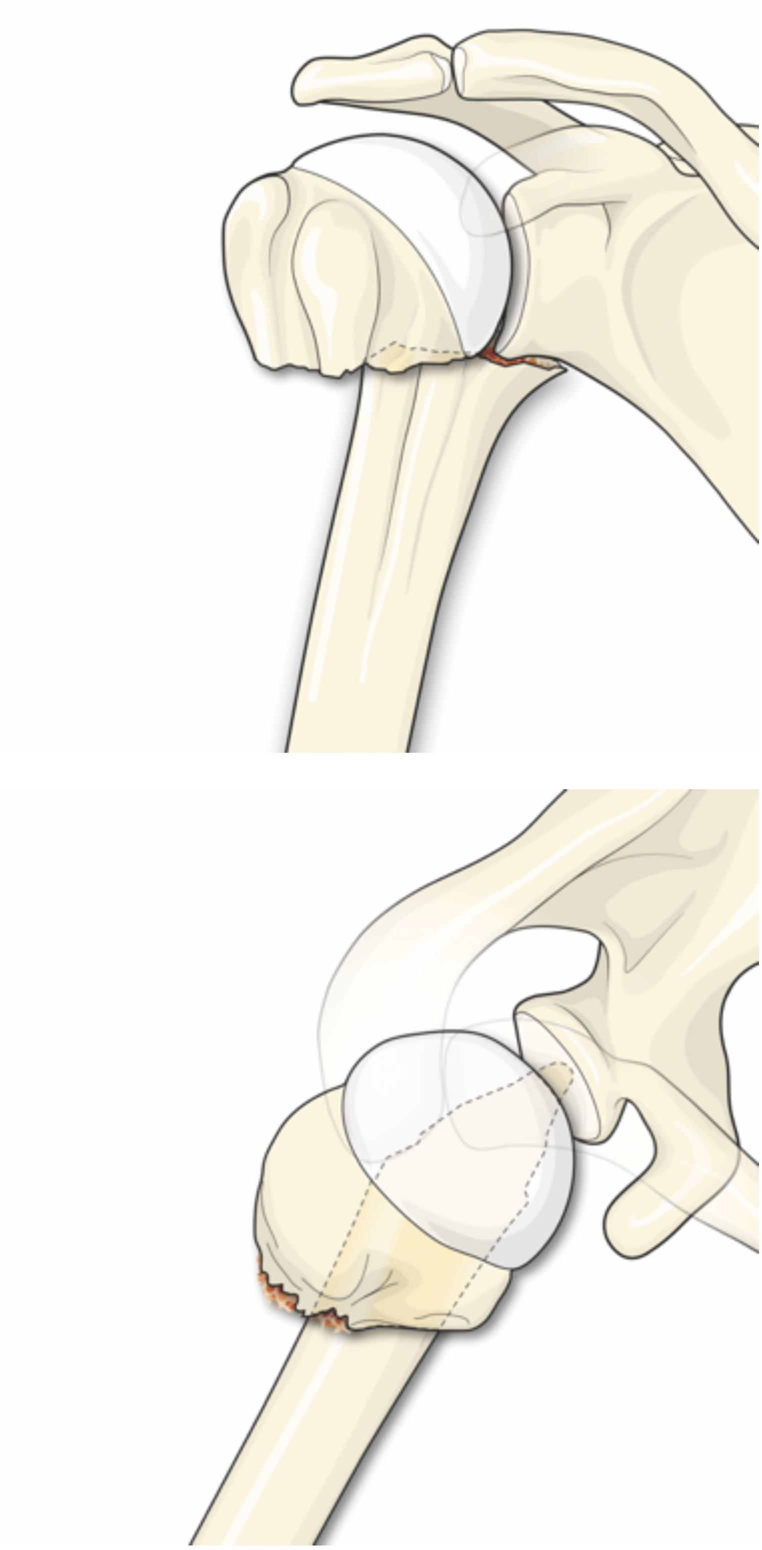


Figure 5-11 AP and modified axial illustrations of an EMS2 fracture.

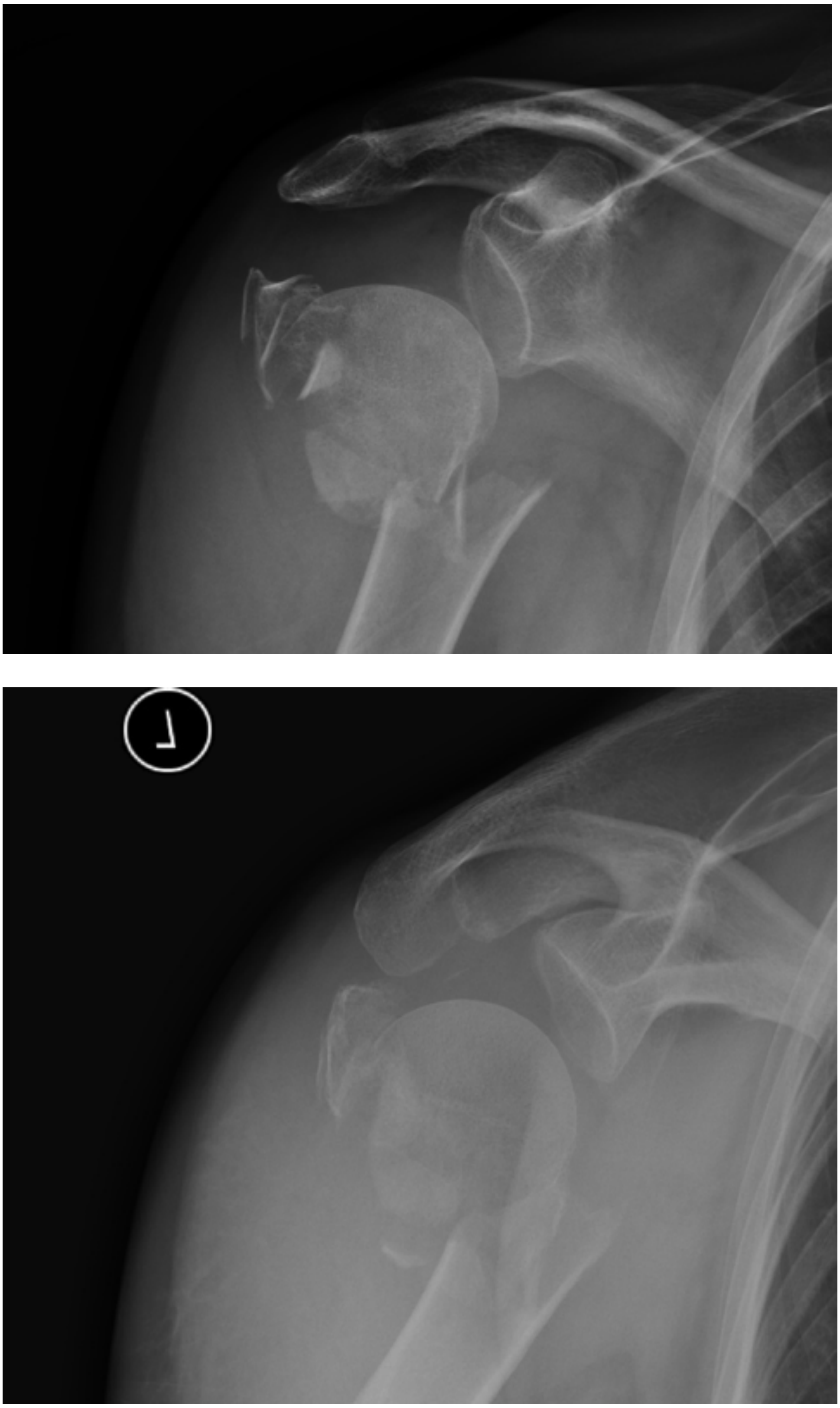


Figure 5-12 AP and modified axial radiographs of an EMS2 fracture.

5.4.8 SUBTUBEROSITY FRACTURES

The mode of failure in these fractures is torsional or bending forces rather than compression. The principal fracture line occurs below the level of the surgical neck and is centred in the distal third of the modified Mullers box. There tends not to be impaction and there may be separation between the fracture fragments. There may by comminution. There is often a long medial metaphyseal spike present on the head fragment. Tuberosity involvement is uncommon. The head angulation is either neutral or varus due to the deforming fore of the intact rotator cuff. There must be displacement between the head and shaft otherwise the fracture should be classified as undisplaced.

5.4.9 **Subtuberosity 1 (ST1)**

These fractures occur below the surgical neck and are centred in the distal third of the Mullers box. Simple fractures may extend distally below the modified Mullers box. Comminution may be present but it does not extend outwith the modified Mullers box. There is no segmental diaphyseal involvement. The fracture line may either be oblique or transverse. Example illustrations and radiographs of this fracture are shown in Figure 5-13 and Figure 5-14.

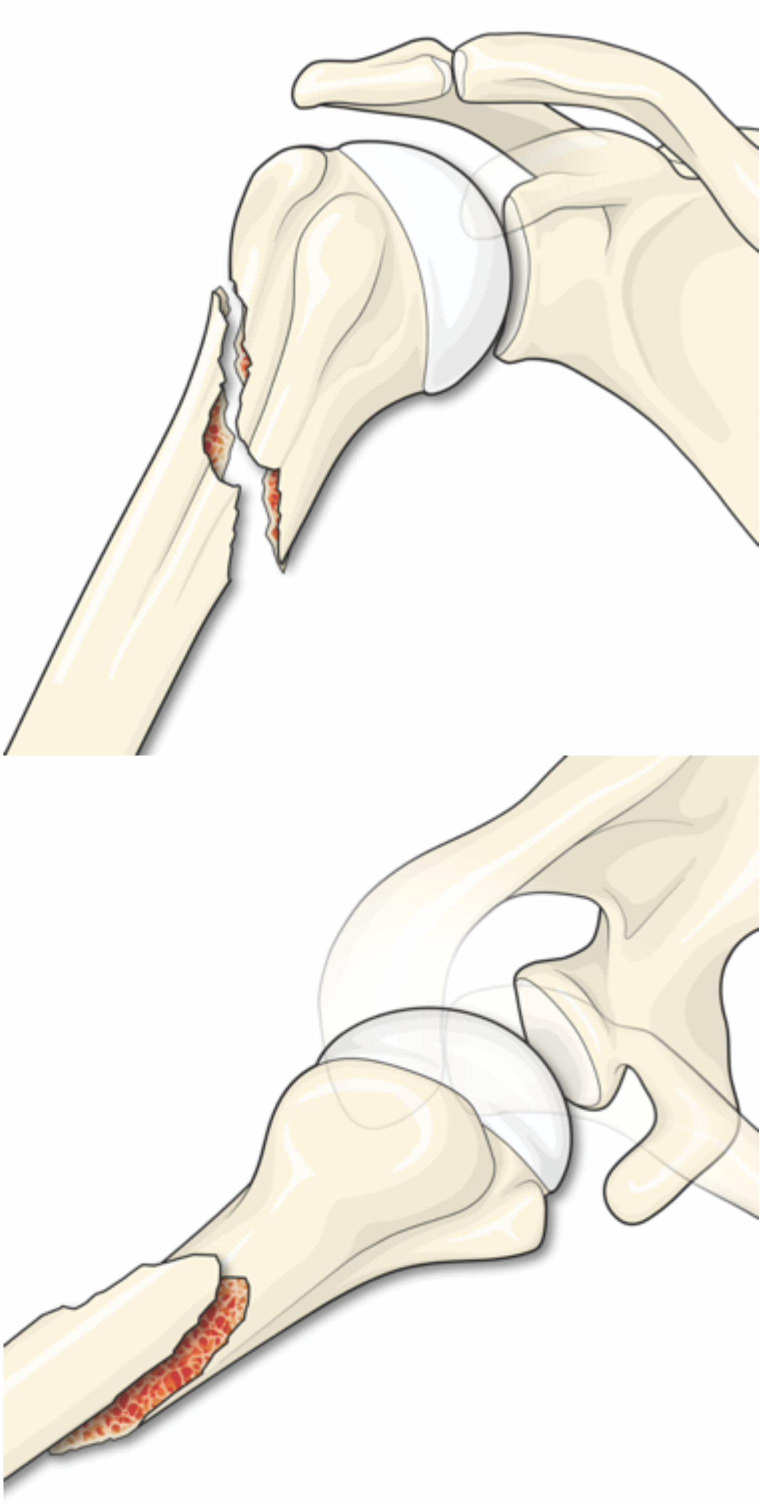


Figure 5-13 AP and modified axial illustrations of an ST1 fracture.

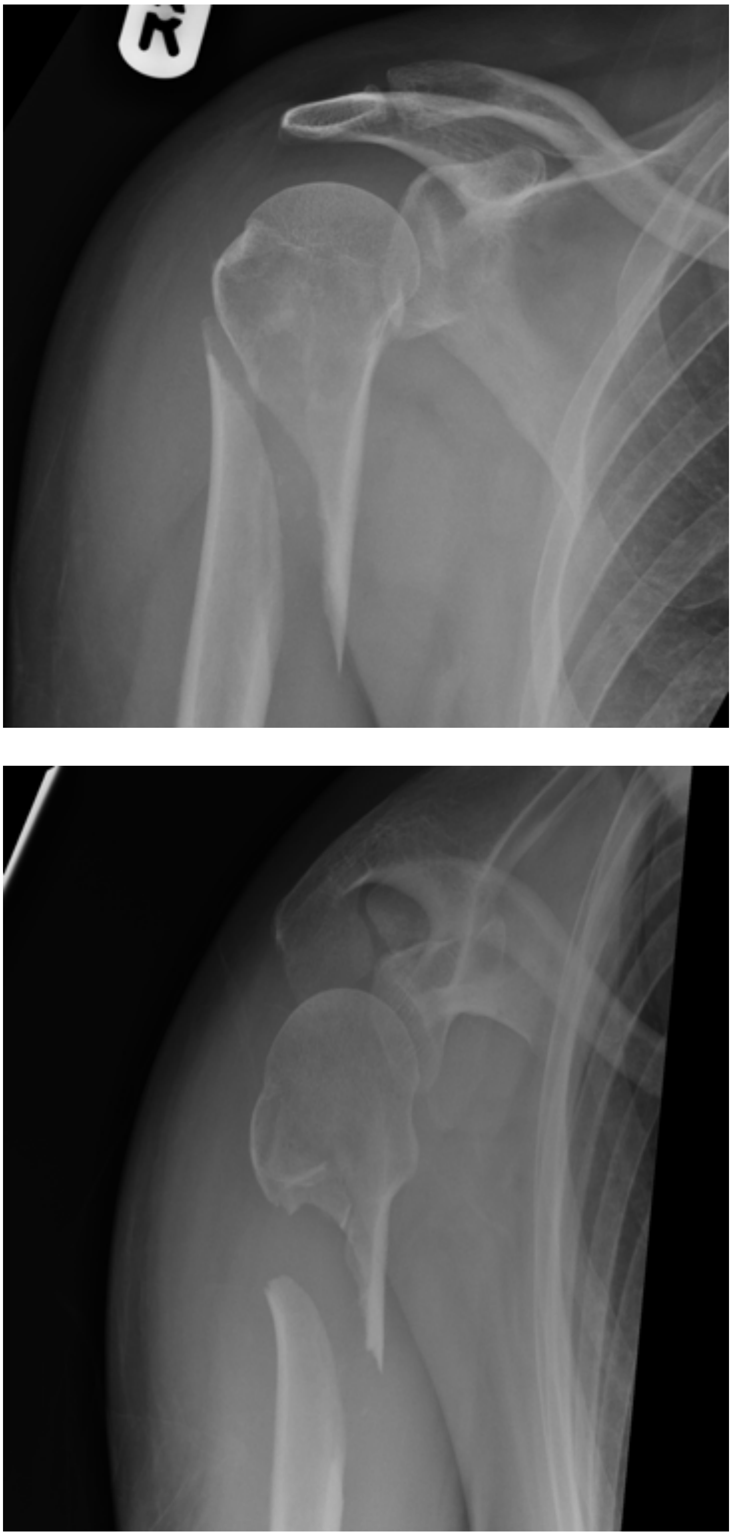


Figure 5-14 AP and modified axial radiographs of an ST1 fracture.

5.4.10 **Subtuberosity 2 (ST2)**

There is a fracture below the surgical neck that is centred in the distal third of the Mullers box. There is segmental diaphyseal comminution extending outwith the modified Mullers box. Example illustrations and radiographs of this fracture are shown in Figure 5-15 and Figure 5-16.

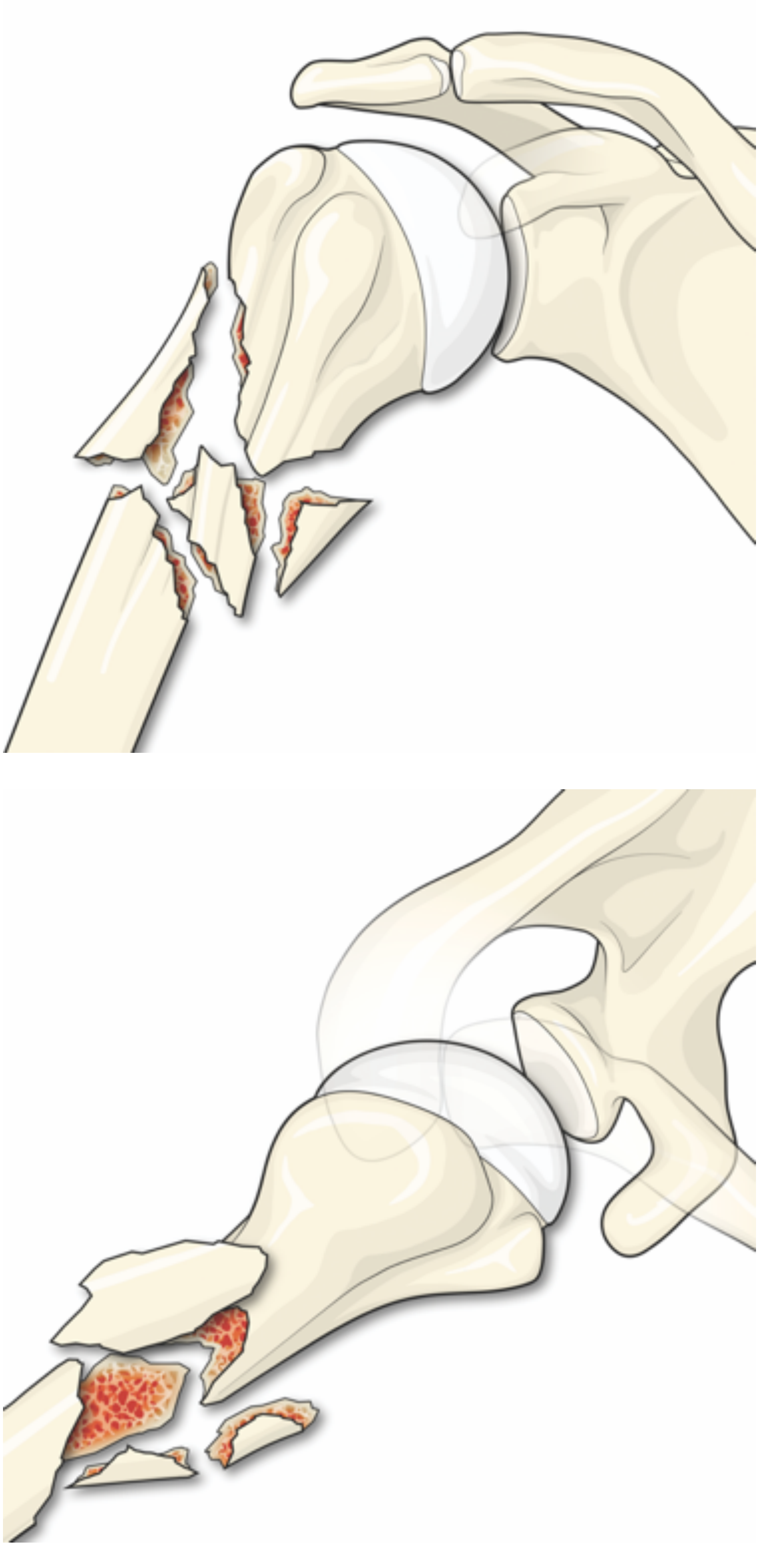


Figure 5-15 AP and modified axial illustrations of an ST2 fracture.

Figure 5-16 AP and modified axial radiographs of an ST2 fracture.

5.4.11 **MEDIAL COMPRESSION FRACTURES**

The plane of fracture in medial compression injuries is at the surgical neck with impaction of the shaft inside the head. The head is rotated into varus and retroversion. The medial calcar is usually attached to the head fragment but in some cases may be comminuted. Medial compression fractures are characterised by superior translation of the shaft as it is driven up into the humeral head. As a result of this, the continuity of the medial ‘gothic arch’ is lost. The ‘gothic arch’ of the normal shoulder is formed by a line drawn along the medial humeral shaft and calcar and a line drawn along the lateral scapular border, which intersect at the inferior articular margin. The shaft is either contained within the head or in end stage fractures may escape anteriorly. There is progressive apex anterior angulation seen on the modified axial radiograph. There may be associated displaced tuberosity fractures, which a thought to represent a more severe end of the spectrum in which undisplaced fractures of the tuberosities open up and displace.

5.4.12 **Medial compression 1 (MC1)**

In these fractures, the deforming force transferred to the proximal humerus is relatively minor. The medial cortex fails at the surgical neck, and the shaft is impacted inside the humeral head. As a result of this, the continuity of the medial 'gothic arch' is lost. In most the calcar remains on the head and the medial cortex of the shaft overlaps and sits just lateral to this. Occasionally, the calcar is comminuted. There may be slight lateral translation of the shaft on the AP radiograph (under 50%). The head angulation is either neutral or may be in slight varus (under 90 degrees in relation to the glenoid). The humeral head retroverts and slight anterior translation (under 50%) and apex anterior angulation is present on the modified axial radiograph. There may posteromedial comminution which is best seen at the base of the greater tuberosity on the modified axial radiograph but there is no displaced tuberosity fracture. The principal neck fracture line tends to run from superolateral to inferomedial. Example illustrations and radiographs of this fracture are shown in Figure 5-17 and Figure 5-18.

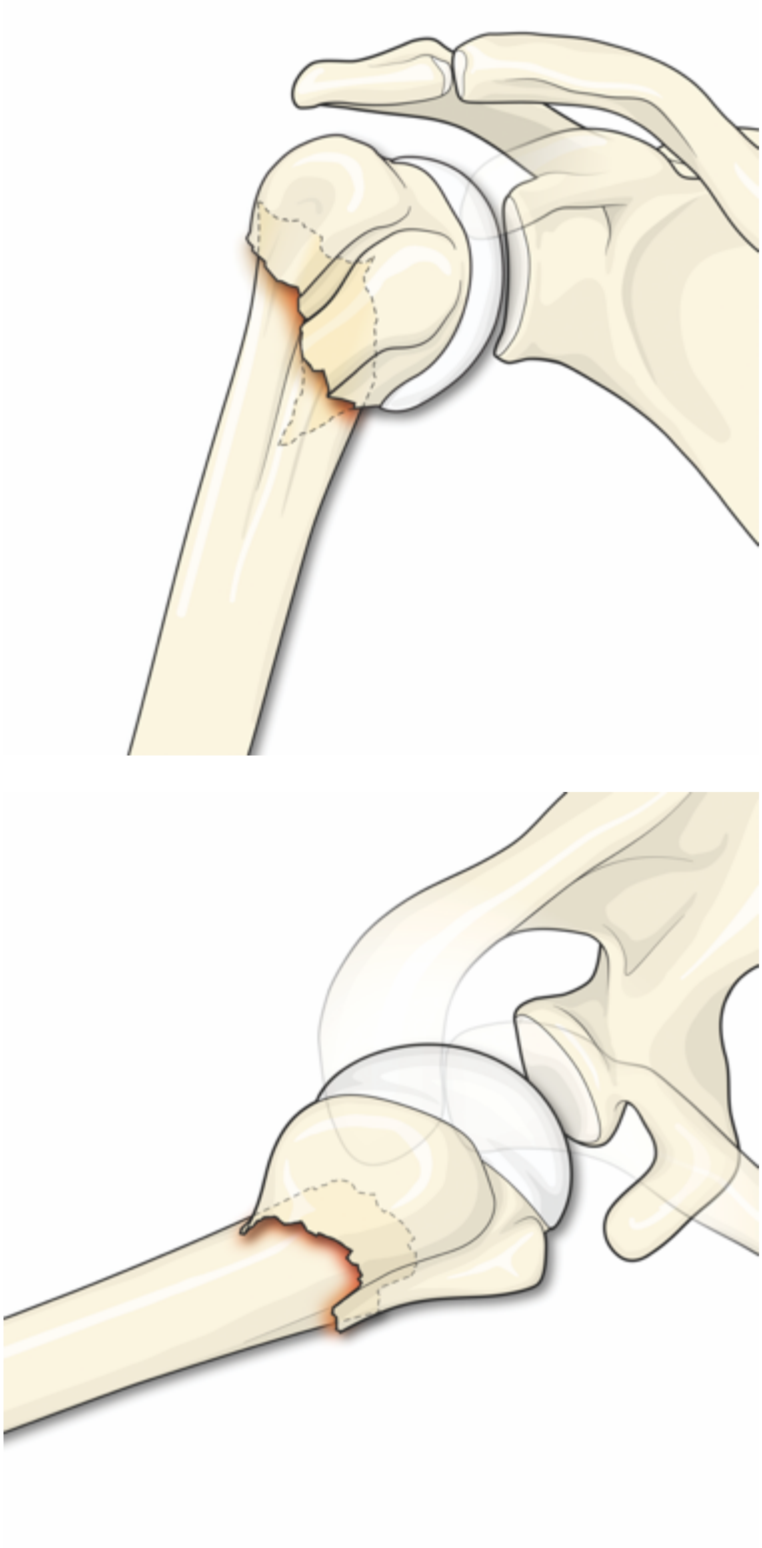
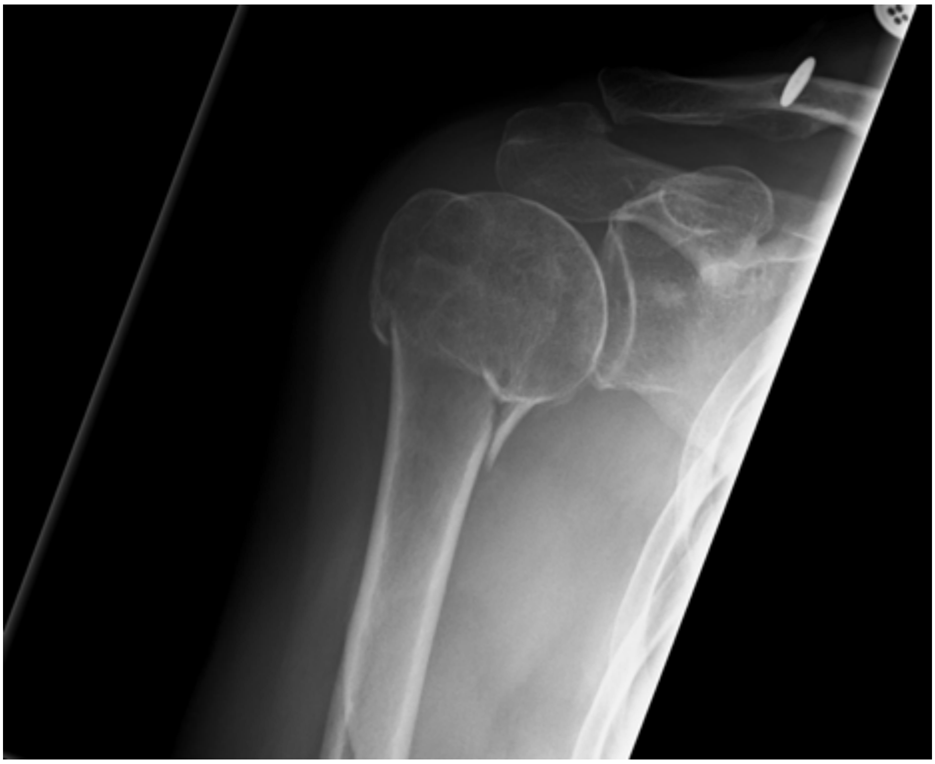


Figure 5-17 AP and modified axial illustrations of an MC1 fracture.



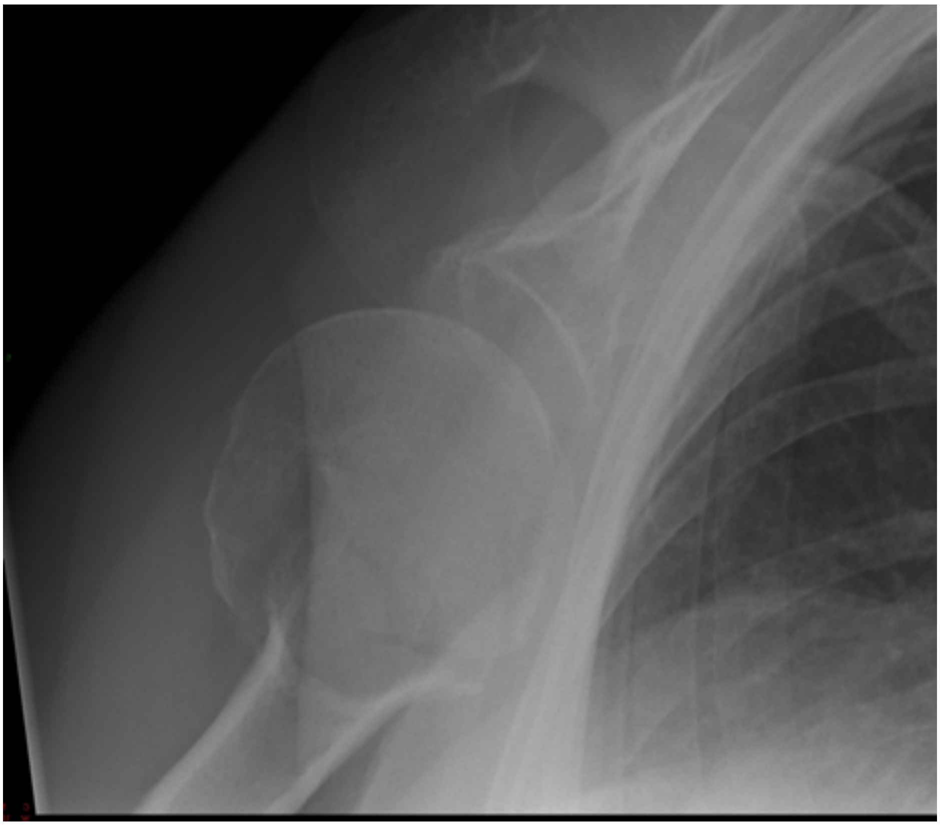


Figure 5-18 AP and modified axial radiographs of an MC1 fracture.

5.4.13 **Medial compression 2 (MC2)**

The medial cortex fails at the surgical neck, and the shaft is impacted inside the humeral head. As a result of this, the continuity of the medial 'gothic arch' is lost. In most cases the calcar remains on the head and the medial cortex of the shaft overlaps and sits just lateral to this. Occasionally, the calcar is comminuted. There may be slight lateral translation of the shaft on the AP radiograph (under 50%). The head angulation is either neutral or may be in slight varus (under 90 degrees in relation to the glenoid). The humeral head retroverts and slight anterior translation (under 50%) and apex anterior angulation is present on the modified axial radiograph. There is posteromedial comminution with an associated displaced fracture to tuberosity segment. There may be subluxation of the humeral head. The principal neck fracture line tends to run from superolateral to inferomedial. Example illustrations and radiographs of this fracture are shown in Figure 5-19 and Figure 5-20.

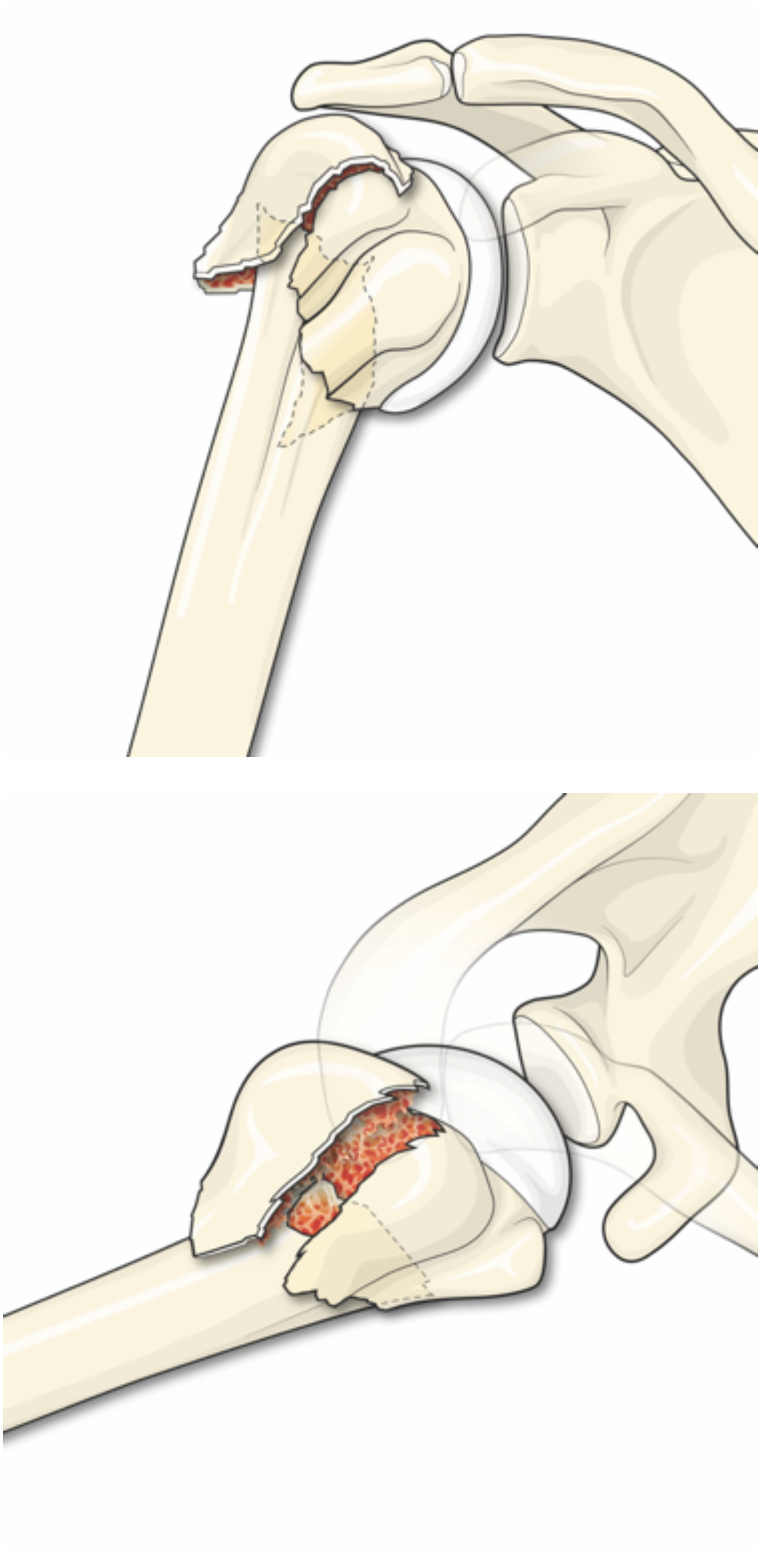


Figure 5-19 AP and modified axial illustrations of an MC2 fracture.

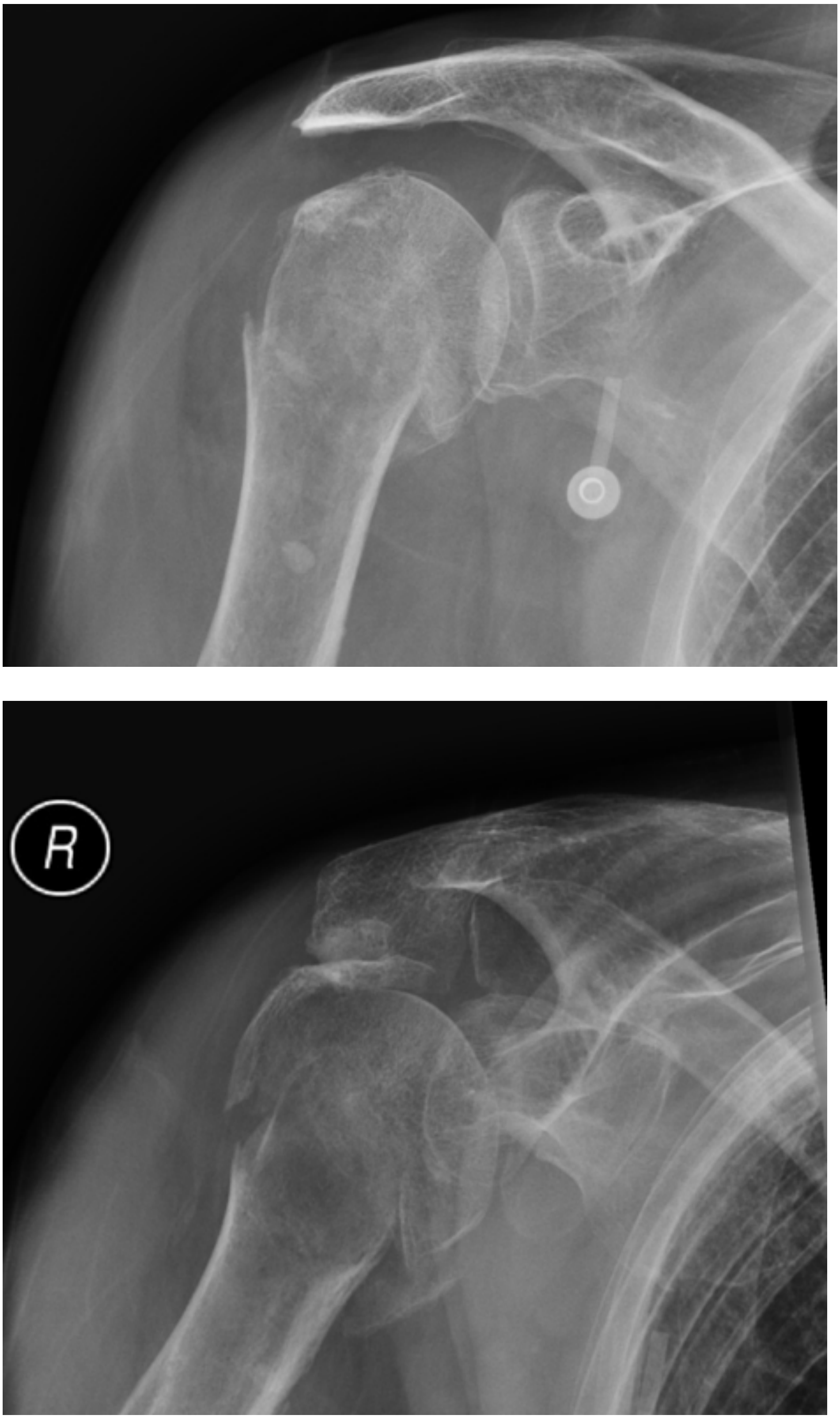


Figure 5-20 AP and modified axial radiographs of an MC2 fracture.

5.4.14 **Medial compression 3 (MC3)**

This represent a progression of the type 1 medial impaction fracture to an unstable fracture pattern. The principal fracture line is at the surgical neck and the shaft is driven superiorly into the head. There is progressive varus deformity of the humeral head and lateral translation of the shaft. The criteria for a medial compression fracture to join this group are over than 50% lateral translation of the shaft in relation to the head or greater than 90 degrees of head angulation. There will usually be slight anterior angulation on the modified axial radiographs but under 50% anterior translation. There may posteromedial comminution which is best seen at the base of the greater tuberosity on the modified axial radiograph but there is no displaced tuberosity fracture. The principal neck fracture line tends to run from superolateral to inferomedial. Example illustrations and radiographs of this fracture are shown in Figure 5-21 and Figure 5-22.

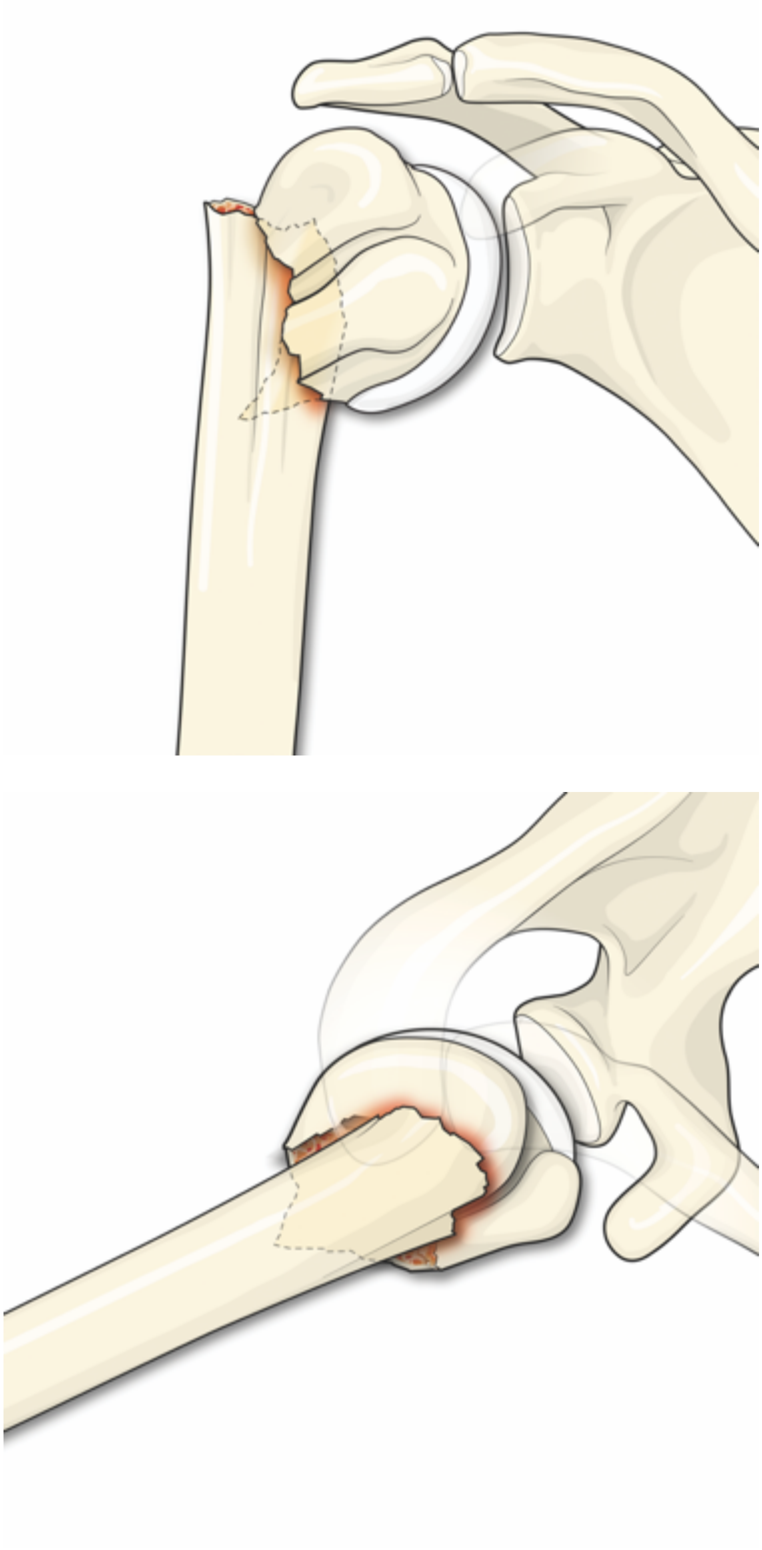


Figure 5-21 AP and modified axial illustrations of an MC3 fracture.

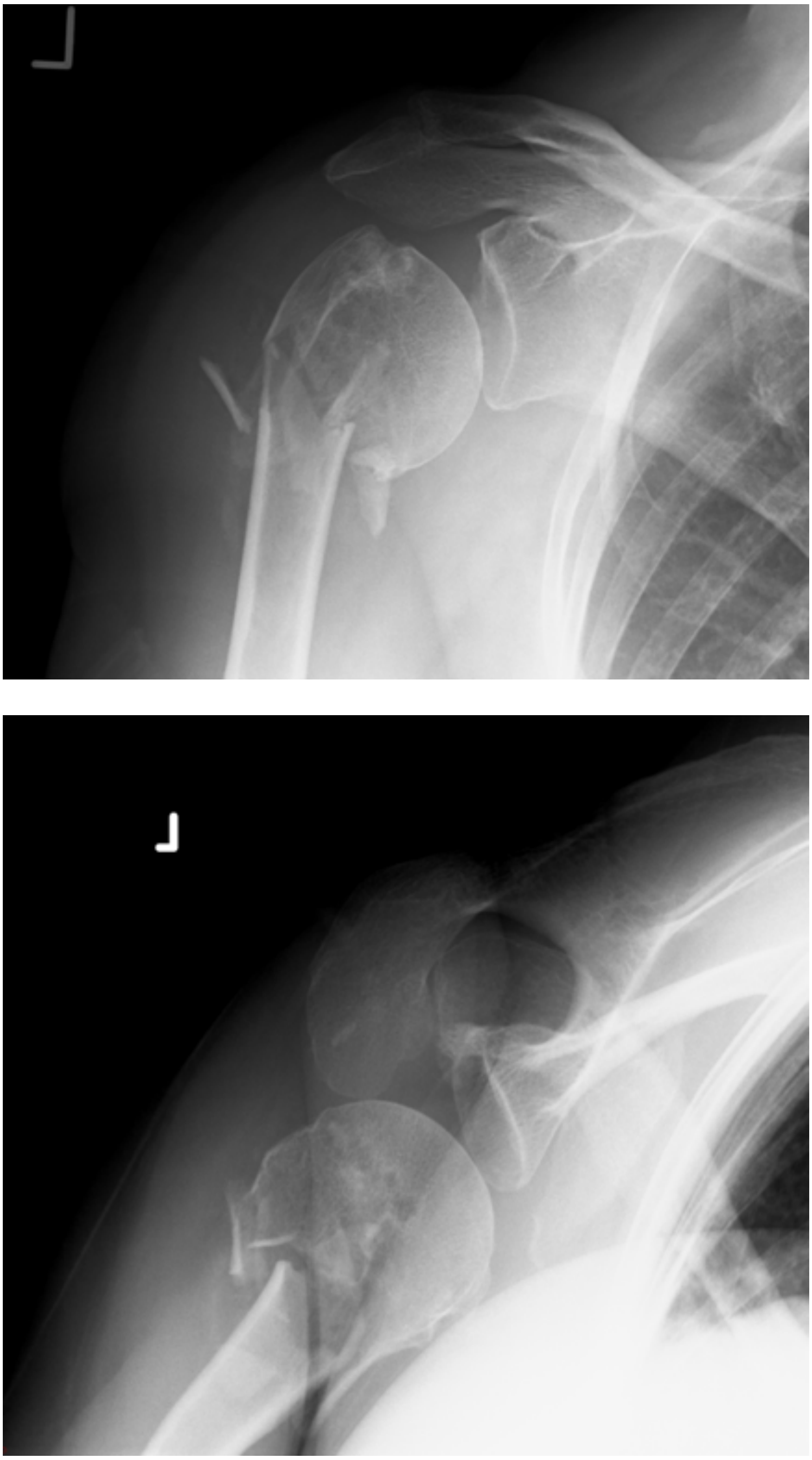


Figure 5-22 AP and modified axial radiographs of an MC3 fracture.

5.4.15 **Medial compression 4 (MC4)**

This represent a progression of the type 1 medial impaction fracture to an unstable fracture pattern. The principal fracture line is at the surgical neck and the shaft is driven further superiorly into the head. There is progressive varus deformity of the humerual head and lateral translation of the shaft. The criteria for a medial compression fracture to join this group are over than 50% lateral translation of the shaft in relation to the head or greater than 90 degrees of head angulation. There will usually be slight anterior angulation on the modified axial radiographs but under 50% anterior translation. There is posteromedial comminution with an associated displaced fracture to tuberosity segment. The tuberosity is displaced proximally and medially. There is often subluxation of the humeral head. The principal neck fracture line tends to run from superolateral to inferomedial. Example illustrations and radiographs of this fracture are shown in Figure 5-23 and Figure 5-24.

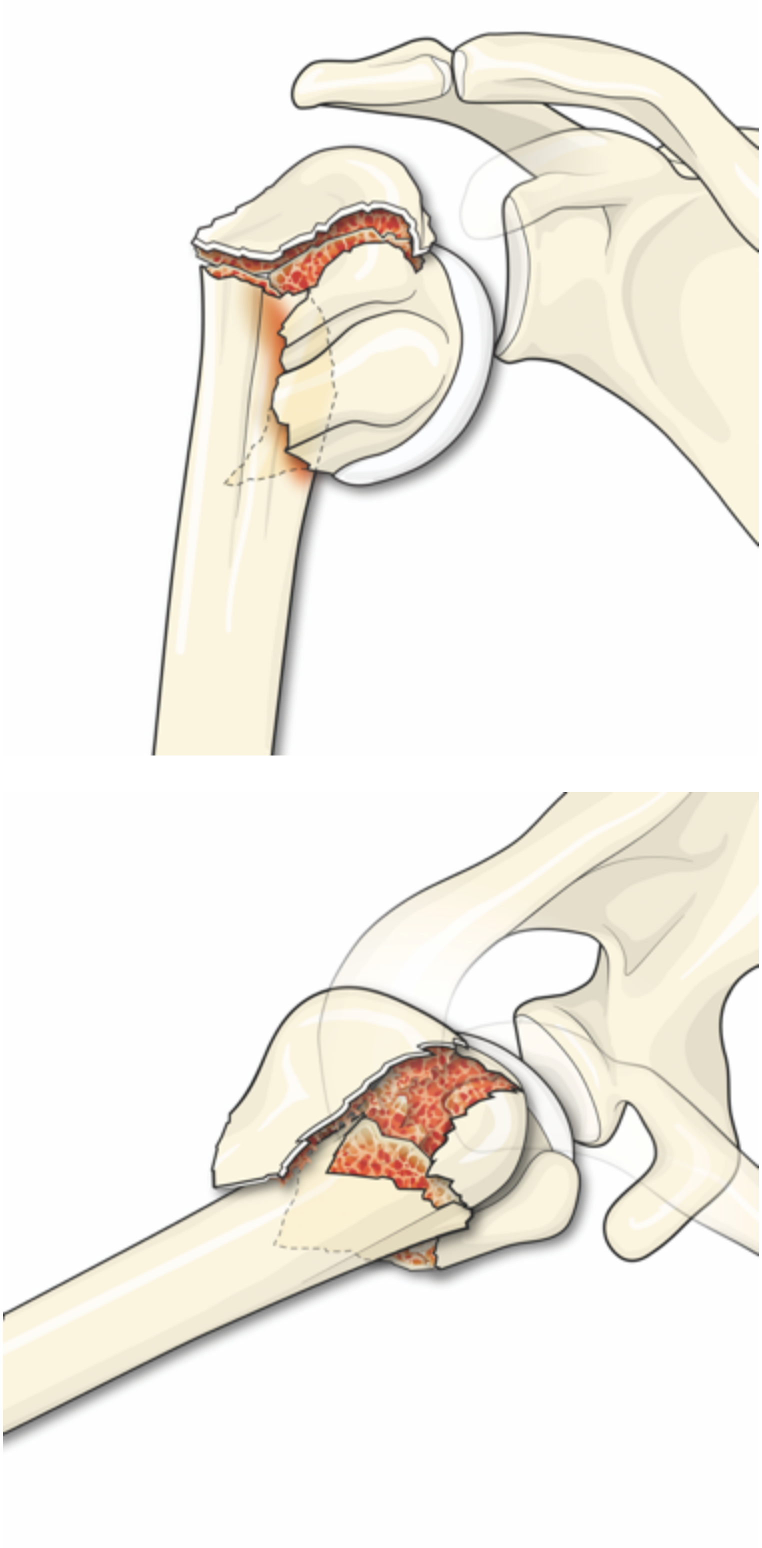


Figure 5-23 AP and modified axial illustrations of an MC4 fracture.

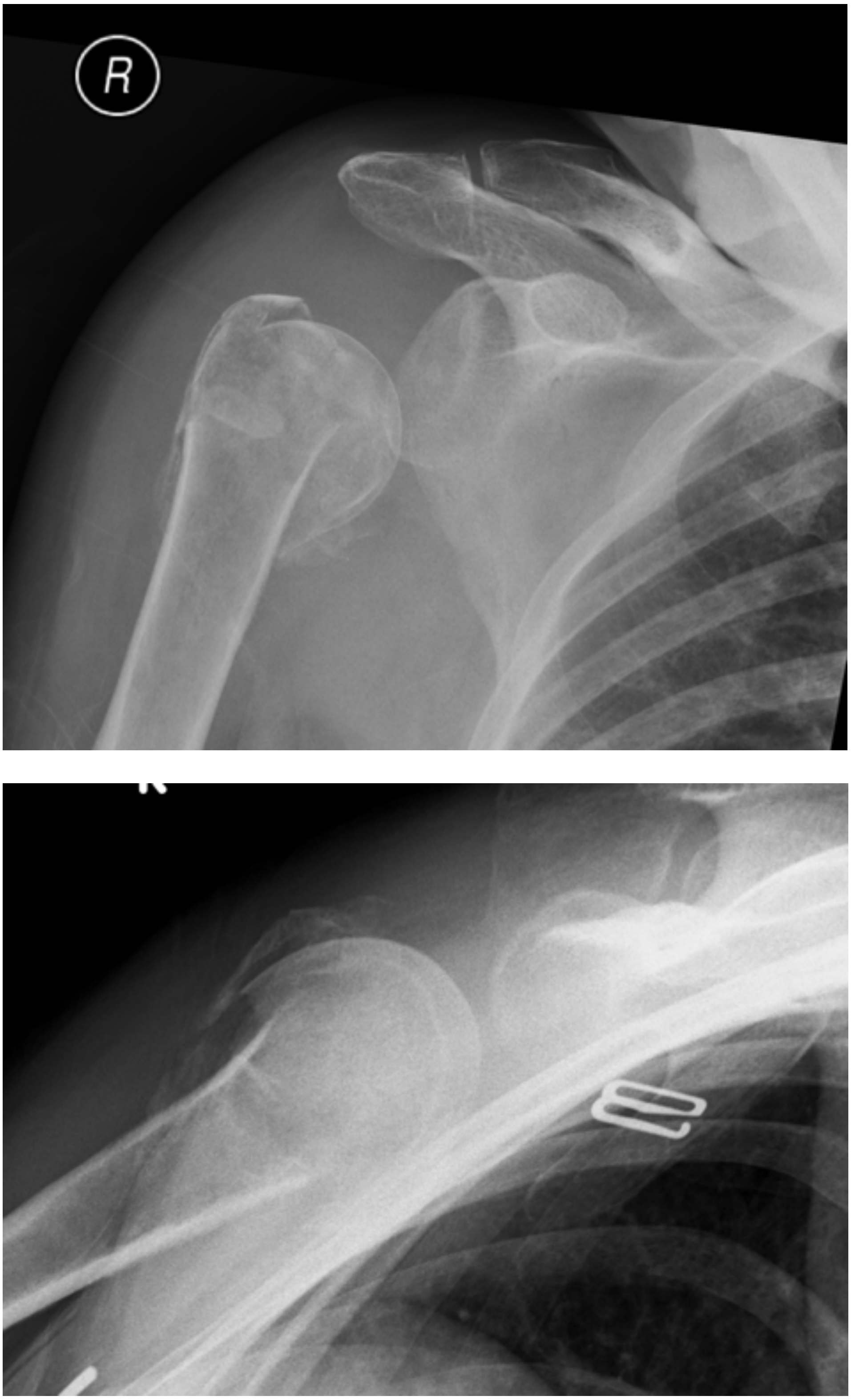


Figure 5-24 AP and modified axial radiographs of an MC4 fracture.

5.4.16 **Medial Compression 5 (MC5)**

This represent a progression of the type 1 medial impaction fracture to an unstable fracture pattern. The principal fracture line is at the surgical neck and the shaft. As the shaft is driven superiorly it escapes from underneath the head and displaces anteriorly. The criteria for a medial compression fracture to join this group are over than 50% anterior translation of the shaft in relation to the head. There may posteromedial comminution which is best seen at the base of the greater tuberosity on the modified axial radiograph but there is on displaced tuberosity fracture. The principal neck fracture line tends to run from superolateral to inferomedial. Example illustrations and radiographs of this fracture are shown in Figure 5-25 and Figure 5-26.

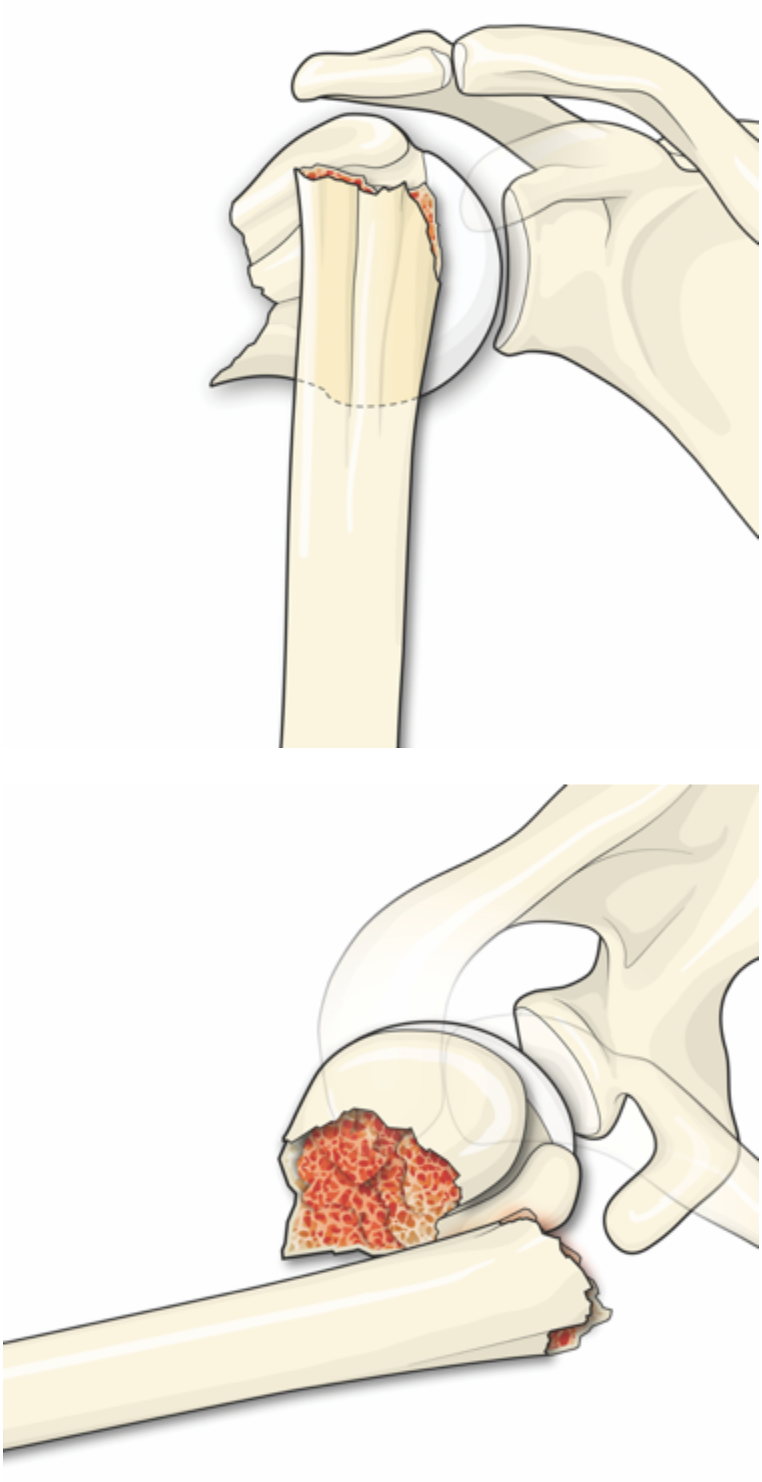


Figure 5-25 AP and modified axial illustrations of an MC5 fracture.

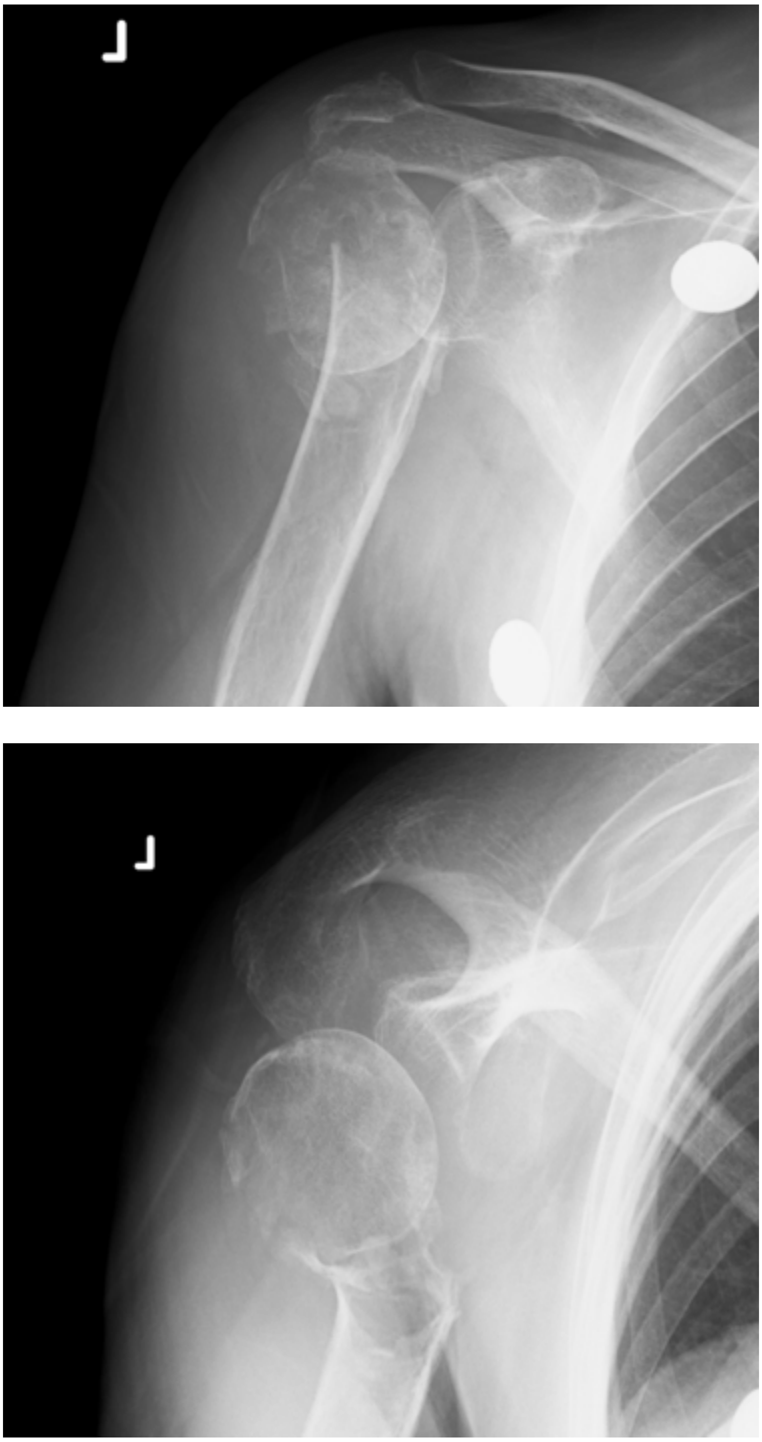


Figure 5-26 AP and modified axial illustrations of an MC5 fracture.

5.4.17 **Medial compression 6 (MC6)**

This represent a progression of the type 1 medial impaction fracture to an unstable fracture pattern. The principal fracture line is at the surgical neck and the shaft. As the shaft is driven superiorly it escapes from underneath the head and displaces anteriorly. The criteria for a medial compression fracture to join this group are over than 50% anterior translation of the shaft in relation to the head. There is a fracture of the tuberosity, equivalent to end stage four part fracture. Example illustrations and radiographs of this fracture are shown in Figure 5-27 and Figure 5-28.

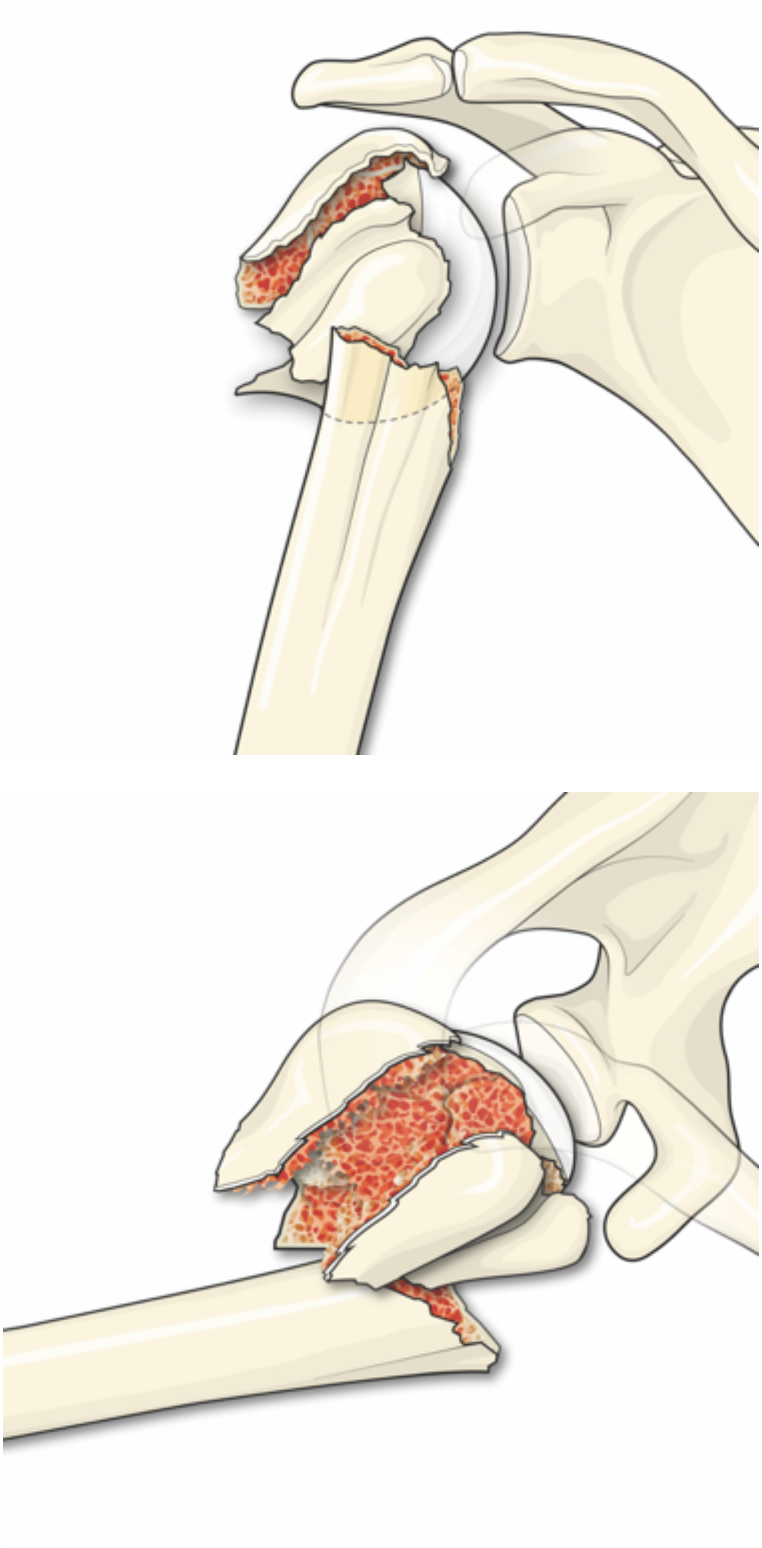


Figure 5-27 AP and modified axial illustrations of an MC6 fracture.

Figure 5-28 AP and modified axial illustrations of an MC6 fracture.

5.4.18 **Fracture dislocation**

This group includes any NHF with an associated dislocation of the glenohumeral joint.

5.4.19 **Unclassifiable fractures**

A fracture that does not meet the criteria of any of the above categories is deemed unclassifiable. The complete classification is summarised in Table 5-1.

Fracture subtype	Head-shaft translation	Head angle	Separation	Tuberosity fracture
Undisplaced				
UD (61)	Nil	Neutral	Nil	Nil
Lateral compression				
LC1 (21)	Nil	Neutral	Nil	Undisplaced fracture
LC2 (22)	Nil	Valgus	Nil	Displaced fracture
LC3 (24)	Under 50%	Valgus	Nil	Displaced fracture
EMS				
EMS1 (26)	Under 50%	Neutral	Nil	Variable
EMS2 (23)	Over 50%	Neutral	Nil	Variable
Medial compression				
MC1 (32)	Under 50%	Varus	Nil	Nil or undisplaced
MC2 (322)	Under 50%	Varus	Nil	Displaced
MC3 (33)	Lateral over 50%	Over 90 degrees	Nil	Nil or undisplaced
MC4 (34)	Lateral over 50%	Over 90 degrees	Nil	Displaced
MC5 (35)	Anterior over 50%	Variable	Nil	Nil or undisplaced
MC6 (36)	Anterior over 50%	Variable	Nil	Displaced
Subtuberosity				
ST1 (42)	Variable	Neutral	Variable	Variable
ST2 (43)	Variable	Neutral	Variable	Variable

Table 5-1 Summary of the fracture classification. The fractures in rows shaded green are ‘stable’ fractures and the fractures in rows shaded red are ‘unstable’ according to the definition of stability described in section 5.3.3.

5.5 CHAPTER DISCUSSION

This chapter describes the development of a novel classification which was designed to be straightforward to use and include all of the commonly encountered, clinically relevant fracture subtypes. The classification is based around prognostic factors identified in CHAPTER 4 so might help predict outcome and potentially inform treatment decisions or provide a basis for the subdivision of patients during future studies evaluating the outcome of NHF. Other authors may have arrived at a different final fracture classification however the present classification was intended to meet the criteria set out in section 5.3. The fracture classification is evaluated further in CHAPTER 6 and CHAPTER 7.

CHAPTER 6
EPIDEMIOLOGICAL ANALYSIS OF THE NOVEL FRACTURE CLASSIFICATION

6.1 CHAPTER AIMS

The aim of this chapter is to describe the epidemiological characteristics of NHF according to the novel classification system described in CHAPTER 5. Interobserver reliability and intraobserver reproducibility of the classification are also assessed.

6.2 INTRODUCTION

For the purposes of epidemiological work, fracture classifications allow researchers to *name*, *describe* and *compare* different fracture subtypes within a given classification system. This may improve our understanding of the natural history of different patterns of injury and provide a basis for outcome studies that will in future guide treatment and facilitate service planning.

Review of the published series (CHAPTER 1) highlights the need for a single classification system for NHF and epidemiological investigation in an unselected geographically based population. No previous study has focused on NHF specifically, all include cases of isolated tuberosity fracture.

Existing classifications divide cases into categories based on the pattern, extent and complexity of radiological abnormality but subgroups in one classification do not have a direct equivalent in another - making detailed comparison impossible. To complicate matters, different authors use their own modifications of the Neer and AO classifications which may preclude comparison of studies that have been categorised using the same basic classification system.

In this chapter the epidemiology of patterns of NHF will be investigated for the first time, using the novel classification described in CHAPTER 5, in a prospectively ascertained consecutive series of patients from a well geographically defined population.

The study reported in CHAPTER 3 investigated the epidemiology of NHF in relation to patient age, gender, mode of injury and social deprivation. Other studies looking at medical comorbidities and lifestyle in more detail have identified diabetes mellitus, depression, alcohol consumption and the use of anticonvulsant medication as risk factors for proximal humerus fractures(24, 108, 121, 122). There are no studies describing the prevalence of these factors in NHF. Their prevalence will therefore be investigated as part of the epidemiological study described in this chapter.

6.3 METHODS

6.3.1 **Data collection**

Database 2 was used to examine the epidemiology of NHF between 1st November 2013 and 31st October 2014. The study setting, method of case ascertainment, inclusion criteria and demographic data collected is described in detail in CHAPTER 2.

All of the patients included in this study had a proximal humerus fracture involving the neck of humerus. Patients with a proximal humerus fracture that did not involve the neck of humerus were excluded. Demographic data, which was recorded in database 2, included patient age, gender, mode of injury, deprivation quintile, pre-injury level of independence, smoking status, alcohol consumption and medical comorbidities. This data was obtained from review of the electronic patient records. For smoking status, patients were either classified as current smokers or non smokers. The number of cigarettes smoked per day was not recorded. For alcohol intake patients with a documented history of excess intake were recorded as such. Those without a documented history were recorded as not excess drinkers. This quantity of alcohol intake for each individual patient was not recorded. Patients with the following medical comorbidities were recorded as such if the medical comorbidity was documented in the electronic patient record: cardiac disease, respiratory disease, renal disease, liver disease, active malignancy, diabetes, hypertension, stroke, inflammatory joint disease and mental illness. Patients were either recorded as living independently or as having formalised care assistance of any type. Each fracture was classified according to the novel system described in CHAPTER 5 by the author (EBG).

The classification was assessed using twenty radiographs, selected at random using a computer number generator. These radiographs were independently classified by three orthopaedic registrars on two occasions, separated by a four-week interval in order to determine interobserver reliability and intraobserver reproducibility. The assessors were asked to evaluate three criteria for each fracture. Firstly, they were asked to state whether the fracture was 'stable' or 'unstable' according to the criteria in section 5.3.3. Secondly, they were asked to state which broad group the fracture belonged to according to the criteria in section 5.4 (undisplaced, lateral compression, early medial separation, subtuberosity or medial compression). Finally, they were asked to state the fracture subtype according to the criteria in section 5.4.

6.3.2 **Statistical analysis**

Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington) and SPSS version 21.0 (SPSS, Chicago, Illinois) were used to undertake statistical analysis. Data were checked for normality using the Kolomogorov-Smirnov test. Continuous data were presented in terms of the median, range and interquartile range if asymmetrically distributed, and the mean and standard deviation if symmetrically distributed.

The Mann-Whitney U test was used to compare nonparametric continuous data between dichotomous variables. Groups of categorical variables were compared using the Chi square test.

Fracture incidence was calculated as the number of fractures per 100,000 of population per year (n/100,000/yr). The 95% confidence interval around the rates was estimated using the cumulative Poisson distribution.

Trends in fracture epidemiology were described according to age at the time of fracture, sex, mode of injury, deprivation, level of function, smoking, alcohol and medical comorbidities. Age- and sex-specific facture distribution curves were produced. Fracture distribution curves were originally set out by Court-Brown and Caesar(31). They determined that there were 8 fracture distribution curves that accounted for the female and male incidence of all fractures, and their use is now recognized within fracture epidemiology(2). The curves are a measure of the changing incidence (y axis) with age (x axis). All curves are associated with peaks in incidence, such as unimodal or bimodal.

The Spearman correlation was used to determine the relationship between incidence and deprivation quintile. The "observed proportion" of fractures in each deprivation quintile was calculated by dividing the number of fractures in that quintile by the total number of fractures. The proportion of the population in that quintile was similarly derived. This served as the "expected proportion" in that the null hypothesis was that there was no difference in the proportion of fractures in each quintile. The observed proportion was, therefore, subtracted from the expected proportion to determine the absolute difference in proportion. This is a basic description of the associated chi-square statistic.

Interobserver reproducibility and intraobserver reliability were determined by calculating adjusted kappa coefficients. Values of kappa can range from -1.0 to 1.0, with -1 indicating perfect disagreement below chance, 0.0 indicating agreement equal to chance, and 1 indicating perfect agreement above chance. Landis and Koch have proposed guidelines for interpretation of the adjusted kappa coefficients(123). Values of less than 0.0 indicated poor reliability; 0.00 – 0.20, 0.21 – 0.40, fair reliability; 0.41 -0.60, moderate reliability; 0.61 – 0.80, substantial agreement and 0.81 – 1.0 excellent agreement.

6.4 RESULTS

6.4.1 Population at risk

According to Scottish government sources, the population served by Edinburgh Royal Infirmary was 570,419 in 2014. There were 296,505 females and 273,914 males. Overall, the ratio of females to males was 1.1:1, but this gradually increased to 2.5:1 in patients aged 90 years or more. The detailed age- and gender-related distribution of the Edinburgh, Midlothian and East Lothian population for 2014 is shown diagrammatically in Figure 6-1.

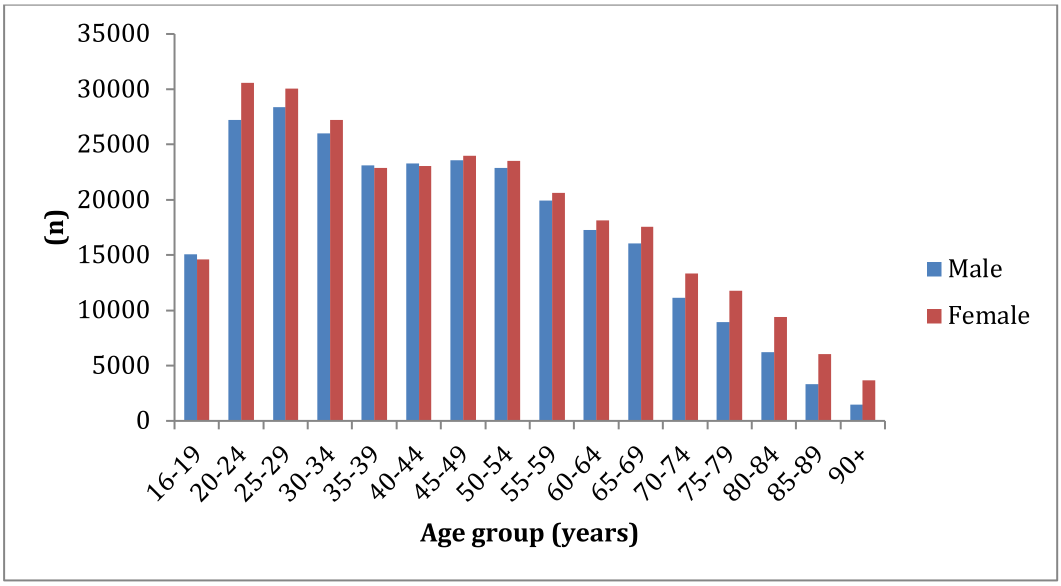


Figure 6-1 The age- and gender-related distribution of adults, aged 16 years or older, served by Edinburgh Royal Infirmary. Data were obtained from the General Register Office for Scotland and represent a mid-year population estimate for 2014 (n=570,419).

There was an uneven distribution of the population served by Edinburgh Royal Infirmary according to deprivation quintile. The overall population at risk was greatest in the most affluent quintile and smallest in the most deprived quintile (Figure 6-2).

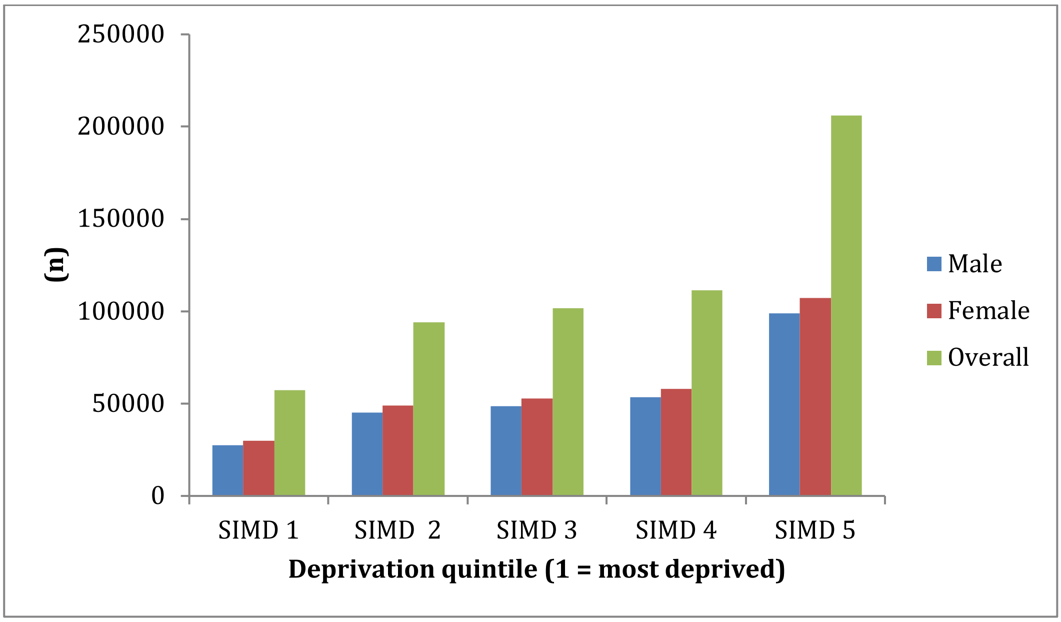


Figure 6-2 Overall number of patients at risk in each deprivation quintile in 2014.

6.4.2 Overall fracture incidence

In 2014, 419 fractures were sustained by 414 patients. Five patients had bilateral simultaneous fractures. The overall incidence of NHF was 72.6 per 100,000 per year.

6.4.3 Sex and age distribution

314 fractures (74.9%) occurred in females and 105 fractures (25.1%) occurred in males. The overall gender specific incidences were 105.9 and 38.3 per 100,000 per year for females and males respectively.

The median age of all patients was 73 years (IQr, 60 – 82) with a range from 18 years to 99 years. The median age of females was 73 years (IQr, 63 – 82 yrs). They represented significantly older group than males, who had a median age of 65 years (IQr, 52 – 81 yrs), (p = 0.034, MWU test).

The fracture distribution curve shows a type F older male and female curve as proposed by Court-Brown and Caesar in 2006 (2) (Figure 6-3). The incidence in females dramatically increased every decade from the age of 40 years, peaking at 583.9 per 100,000 per year in the tenth decade. A steep increase was also seen in males but not until the age of 70 years, peaking at 213.8 per 100,000 per year in the tenth decade.

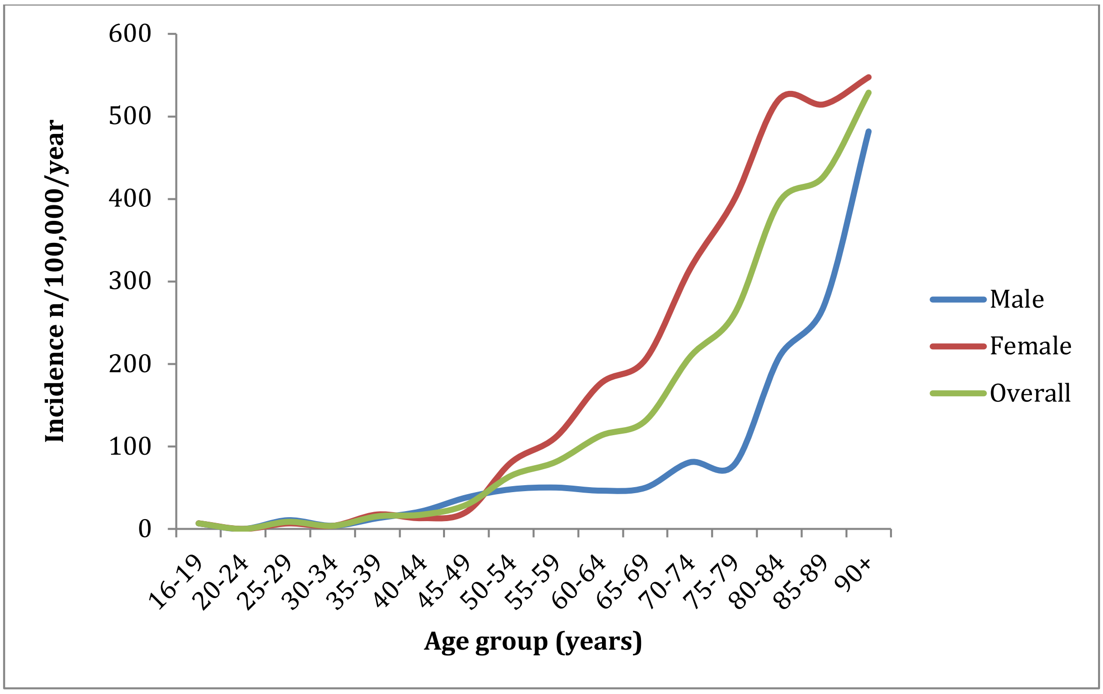


Figure 6-3 The age- gender-related incidence of NHF occurring in adults served by Edinburgh Royal Infirmary.

6.4.4 Mode of injury

Overall, the vast majority of fractures (83.1 percent) were caused by a simple fall (Figure 6-4). The proportion of females sustaining their injuries in this way was greater; 87.6 percent of females as opposed to 69.5 percent of males ($p < 0.001$, Chi-square test). The remaining 16.9 percent of fractures were caused by higher energy injuries. Higher energy injuries occurred more frequently in males and the sex difference was most marked in fractures related to sport (Figure 6-4).

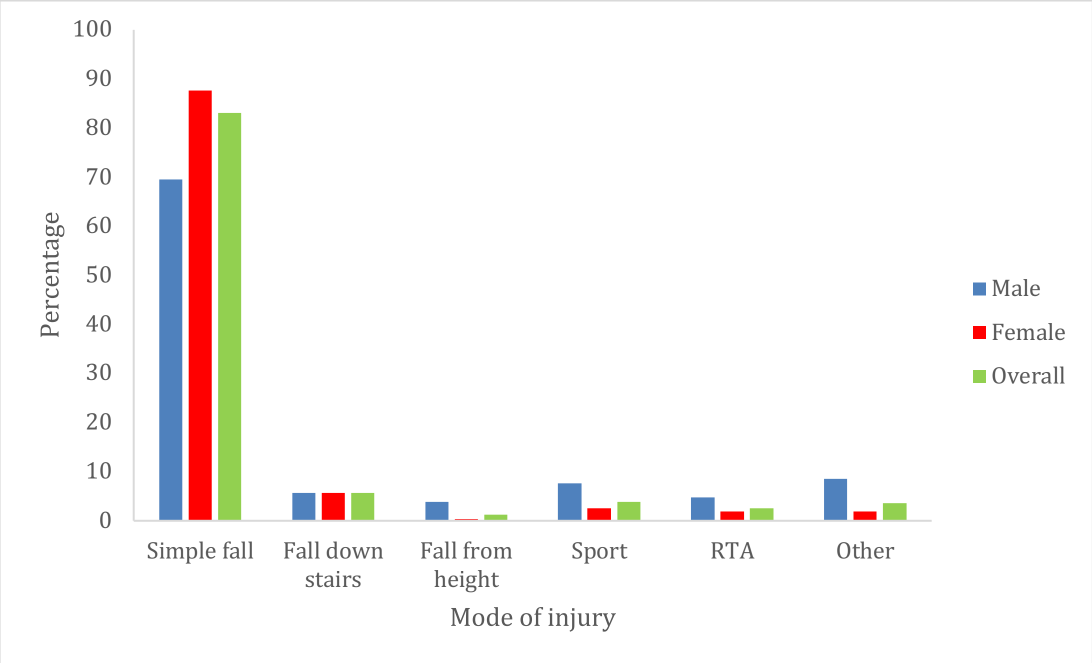


Figure 6-4 Percentage of NHF according to mode of injury and gender.

6.4.5 Deprivation

There was an unequal distribution of fractures according to deprivation (Figure 6-5), with a statistical trend toward an increasing incidence with worsening deprivation (p = 0.037, Spearman correlation coefficient, -0.900). In the second most deprived category, the difference between observed and expected proportions was 4.3% more than expected and in the least deprived group it was 3.7% less than expected (Figure 6-6).

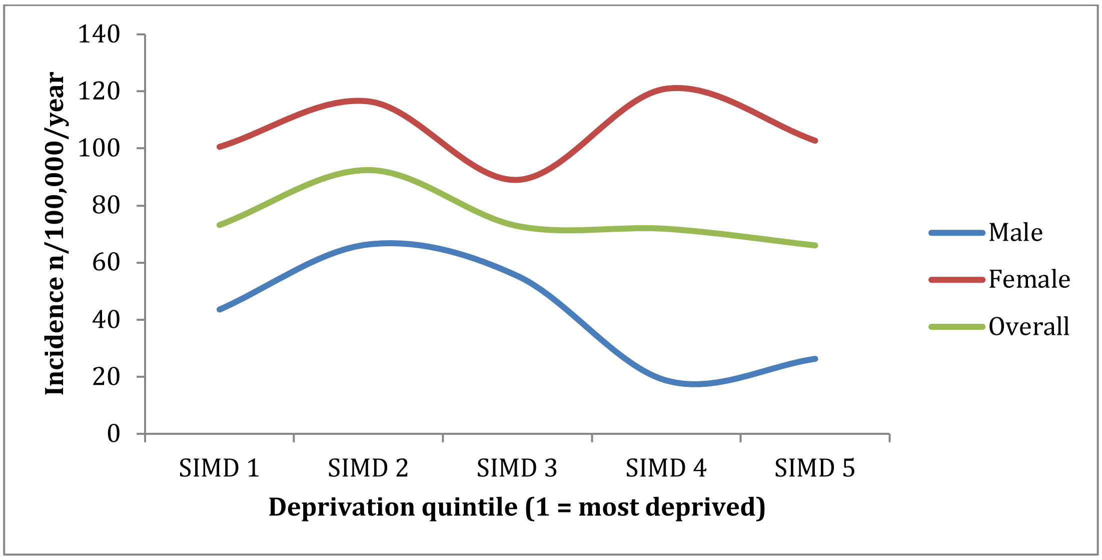


Figure 6-5 The association between NHF incidence and deprivation quintile.

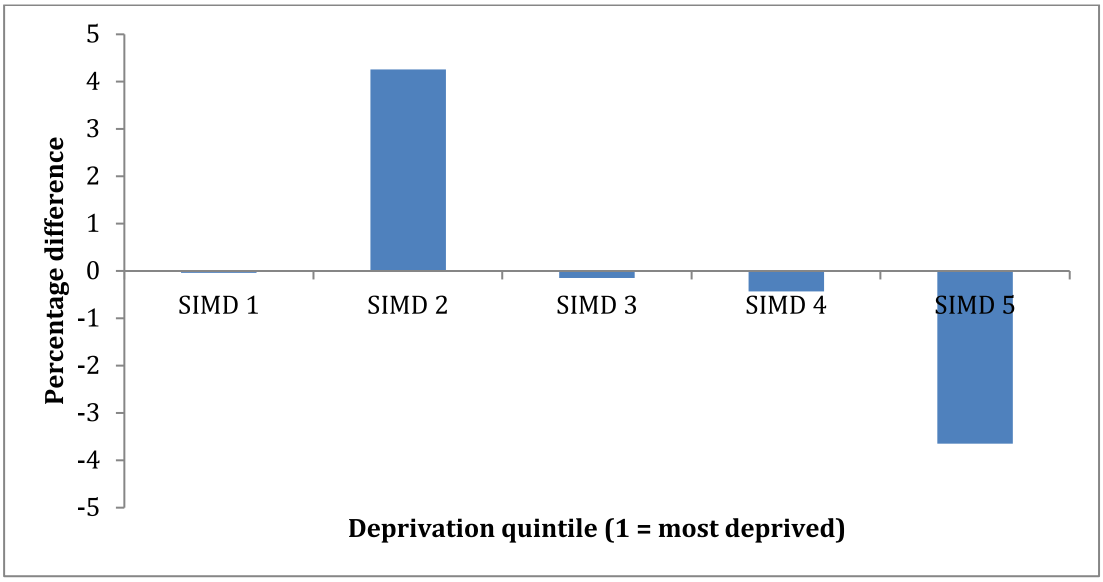


Figure 6-6 Percentage difference between observed and expected proportions of fractures by deprivation quintile.

6.4.6 Level of function, smoking, alcohol and comorbidities

A good level of premorbid function was noted in the majority of patients with 78.1 percent living independently prior the injury. Smoking, alcohol excess and liver disease were more prevalent in males (Table 6-1). The were no differences in the prevalence of the other comorbidities between genders (Table 6-1).

Comorbidity	Number of fractures (%)	Male	Female	p value
Smoking	82 (20.4)	31	51	0.002*
Alcohol excess	96 (22.9)	39	57	<0.001*
Cardiac disease	80 (19.1)	23	57	0.397
Respiratory disease	46 (11.0)	14	32	0.373
Renal disease	32 (7.6)	9	23	0.677
Liver disease	22 (5.3)	10	12	0.023*
Malignancy	56 (13.3)	13	43	0.732
Diabetes	57 (13.6)	15	42	0.814
Hypertension	138 (32.9)	31	107	0.39
Stroke	22 (5.3)	7	15	0.452
Inflammatory joint disease	8 (1.9)	1	7	0.408
Mental illness	104 (24.8)	23	81	0.424

Table 6-1 Prevalence of smoking, alcohol and medical comorbidities.

6.4.7 **Fracture classification epidemiology**

Undisplaced fractures were uncommon, at 1.58% of the fracture population. Lateral compression fractures accounted for 23.2% and early medial separation fractures accounted for 8.6%. Medial compression fractures were the most common at 46.1%, over half of which were unstable. Subtuberosity fractures accounted for 13.8% of the population. 2.4 % of fractures had an associated glenohumeral joint dislocation and 3.8% were unclassifiable. Overall 56.1% of fractures were stable and 37.7% were unstable (Table 6-2).

Lateral compression fractures were common and the medial hinge was intact in the majority of cases. Of the lateral compression fractures with an intact medial hinge, half had head collapse and half did not. Lateral compression fractures tended to occur in younger patients with a median age of 64 years, compared to 73 years for the overall NHF population.

Early medial separation fractures were relatively uncommon and the majority of these injuries were stable. Six out of the 36 early medial separation fractures (16.7%) had an associated displaced tuberosity fracture.

Medial compression fractures accounted for 46.1% of fracture and approximately half of these injuries were unstable. Within the stable injuries, only 10.1% had an associated displaced tuberosity fracture. Within the unstable fractures approximately 50% were shaft anterior subtype and 50% were high lateral shaft subtype. Overall, a greater proportion of the female patients had a medial compression fracture.

Just over one third of the subtuberosity fractures had segmental comminution involving the humeral diaphysis. Overall, a greater proportion of the male patients had a subtuberosity fracture (Table 6-2).

Each fracture subtype occurred predominantly due to simple falls (Table 6-3). The distribution of fracture subtypes according to social deprivation is shown in Table 6-4.

Fracture subtype	Number of fractures (%)	Incidence (/100,000/year)	Median age (range)	Male	Female	F:M ratio
Undisplaced						
UD (61)	9 (2.1)	1.58	71 (26-92)	0	9	No males
Lateral compression	97 (23.2)	17.01	64 (29-92)	24	73	3.04
LC1 (21)	36 (8.6)	6.31	58 (54-83)	10	26	2.6
LC2 (22)	38 (9.1)	6.66	66 (29-90)	10	28	2.8
LC3 (24)	23 (5.5)	4.03	76 (50-92)	4	19	4.75
EMS	36 (8.6)	6.31	74 (49-88)	8	28	3.5
EMS1 (26)	30 (7.2)	5.26	72 (49-88)	8	22	2.75
EMS2 (23)	6 (1.4)	1.05	81 (77-88)	0	6	No males
Medial compression	193 (46.1)	33.83	77 (19-99)	40	153	3.825
MC1 (32)	89 (21.2)	15.6	77 (18-98)	18	71	3.94
MC2 (322)	10 (2.4)	1.75	78 (55-89)	2	8	4.00
MC3 (33)	28 (6.7)	4.91	79 (46-98)	7	21	3.00
MC4 (34)	21 (5)	3.68	78 (49-86)	3	18	6.00
MC5 (35)	22 (5.3)	3.86	73 (44-98)	6	16	2.67
MC6 (36)	23 (5.5)	4.03	83 (56-99)	4	19	4.75
Subtuberosity	58 (13.8)	10.17	69 (26-89)	23	35	1.52
ST1 (42)	36 (8.6)	6.31	71 (26-89)	16	20	1.25
ST2 (43)	22 (5.3)	3.86	63 (38-86)	7	15	2.14
All stable	235 (56.1)	41.2	70 (18-98)	52	183	3.52
All unstable	158 (37.7)	27.7	75 (26-99)	43	115	2.67
Fracture dislocation						
FD (50)	10 (2.4)	1.75	64 (28-87)	5	5	1.00
Unclassifiable						
UN (71)	16 (3.8)	2.8	74 (37-92)	5	11	2.2
Total	**419 (100)**	**73.45**	**73 (18-99)**	**105**	**314**	**2.99**

Table 6-2 The number, incidence, mean age and gender ratio of fractures according to the novel classification system.

Fracture subtype	Simple fall	Fall down stairs	Fall from height	Sport	RTA	Other	Total
Undisplaced							
UD (61)	8 (88.9)	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	9
Lateral compression	79 (82.3)	3 (3.1)	2 (2.1)	7 (7.3)	2 (2.1)	3 (3.1)	96
LC1 (21)	29 (80.6)	1 (2.8)	0 (0)	4 (11.1)	1 (2.8)	1 (2.8)	36
LC2 (22)	31 (81.6)	2 (5.3)	2 (5.3)	1 (2.6)	1 (2.6)	1 (2.6)	38
LC3 (24)	19 (86.4)	0 (0)	0 (0)	2 (9.1)	0 (0)	1 (4.5)	22
EMS	32 (91.4)	1 (2.9)	1 (2.9)	1 (2.9)	0 (0)	0 (0)	35
EMS1 (26)	26 (89.7)	1 (3.4)	1 (3.4)	1 (3.4)	0 (0)	0 (0)	29
EMS2 (23)	6 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6
Medial compression	175 (85.8)	15 (7.4)	0 (0)	3 (1.5)	5 (2.5)	6 (2.9)	204
MC1 (32)	67 (90.5)	1 (1.4)	0 (0)	2 (2.7)	2 (2.7)	2 (2.7)	74
MC2 (322)	6 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6
MC3 (33)	34 (91.9)	3 (8.1)	0 (0)	0 (0)	0 (0)	0 (0)	37
MC4 (34)	11 (73.3)	1 (6.7)	0 (0)	1 (6.7)	1 (6.7)	1 (6.7)	15
MC5 (35)	31 (79.5)	5 (12.8)	0 (0)	0 (0)	1 (2.6)	2 (5.1)	39
MC6 (36)	26 (78.8)	5 (15.2)	0 (0)	0 (0)	1 (3)	1 (3)	33
Subtuberosity	44 (75.9)	5 (8.6)	2 (3.4)	3 (5.2)	0 (0)	4 (6.9)	58
ST1 (42)	25 (69.4)	3 (8.3)	2 (5.6)	2 (5.6)	0 (0)	4 (11.1)	36
ST2 (43)	19 (86.4)	2 (9.1)	0 (0)	1 (4.5)	0 (0)	0 (0)	22
All stable	186 (86.9)	5 (2.3)	3 (1.4)	11 (5.1)	4 (1.9)	5 (2.3)	214
All unstable	152 (80.9)	19 (10.1)	2 (1.1)	4 (2.1)	3 (1.6)	8 (4.3)	188
Fracture dislocation							
FD (50)	5 (50)	0 (0)	0 (0)	0 (0)	3 (30)	2 (20)	10
Unclassifiable							
UN (71)	5 (71.4)	0 (0)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	7
Total	**348 (83.1)**	**24 (5.7)**	**5 (1.2)**	**16 (3.8)**	**11 (2.6)**	**15 (3.6)**	**419**

Table 6-3 Mode of injury according to the novel fracture classification.

Fracture subtype	DQ 1	DQ 2	DQ 3	DQ 4	DQ 5	Total
Undisplaced						
UD (61)	2 (22.2)	0 (0)	2 (22.2)	3 (33.3)	2 (22.2)	9
Lateral compression	5 (5.2)	22 (22.9)	20 (20.8)	16 (16.7)	33 (34.4)	96
LC1 (21)	2 (5.6)	10 (27.8)	7 (19.4)	5 (13.9)	12 (33.3)	36
LC2 (22)	1 (2.6)	9 (23.7)	6 (15.8)	9 (23.7)	13 (34.2)	38
LC3 (24)	2 (9.1)	3 (13.6)	7 (31.8)	2 (9.1)	8 (36.4)	22
EMS	4 (11.4)	6 (17.1)	6 (17.1)	9 (25.7)	10 (28.6)	35
EMS1 (26)	3 (10.3)	5 (17.2)	5 (17.2)	9 (31)	7 (24.1)	29
EMS2 (23)	1 (16.7)	1 (16.7)	1 (16.7)	0 (0)	3 (50)	6
Medial compression	21 (10.3)	41 (20.1)	32 (15.7)	39 (19.1)	71 (34.8)	204
MC1 (32)	8 (10.8)	16 (21.6)	13 (17.6)	15 (20.3)	22 (29.7)	74
MC2 (322)	2 (33.3)	0 (0)	1 (16.7)	1 (16.7)	2 (33.3)	6
MC3 (33)	1 (2.7)	4 (10.8)	6 (16.2)	8 (21.6)	18 (48.6)	37
MC4 (34)	1 (6.7)	6 (40)	2 (13.3)	1 (6.7)	5 (33.3)	15
MC5 (35)	4 (10.3)	7 (17.9)	7 (17.9)	10 (25.6)	11 (28.2)	39
MC6 (36)	5 (15.2)	8 (24.2)	3 (9.1)	4 (12.1)	13 (39.4)	33
Subtuberosity	9 (15.5)	15 (25.9)	12 (20.7)	7 (12.1)	15 (25.9)	58
ST1 (42)	7 (19.4)	8 (22.2)	9 (25)	4 (11.1)	8 (22.2)	36
ST2 (43)	2 (9.1)	7 (31.8)	3 (13.6)	3 (13.6)	7 (31.8)	22
All stable	20 (9.3)	43 (20.1)	41 (19.2)	44 (20.6)	66 (30.8)	214
All unstable	21 (11.2)	41 (21.8)	31 (16.5)	30 (16)	65 (34.6)	188
Fracture dislocation						
FD (50)	1 (10)	3 (30)	1 (10)	3 (30)	2 (20)	10.00
Unclassifiable						
UN (71)	0 (0)	0 (0)	1 (14.3)	3 (42.9)	3 (42.9)	7
Total	**42 (10)**	**87 (20.8)**	**74 (17.7)**	**80 (19.1)**	**136 (32.5)**	**419**

Table 6-4 Deprivation quintile according to the novel fracture classification.

6.4.8 Interobserver reliability and intraobserver reproducibility.

When raters were asked to state whether each fracture was ‘stable’ or ‘unstable’ according to the criteria in section 5.3.3 the interobserver kappa coefficient was 0.67 (0.41 – 0.93) and the mean intraobserver kappa coefficient was 0.67 (0.34 – 0.97).

When raters were asked to state which broad group the fracture belonged to according to the criteria in section 5.4 (undisplaced, lateral compression, early medial separation, subtuberosity or medial compression) the interobserver kappa coefficient was 0.75 (0.58 – 0.92) and the mean intraobserver kappa coefficient was 0.81 (0.61 – 1.0).

When raters were asked to state the fracture subtype according to the criteria in section 5.4 the interobserver kappa coefficient 0.53 (0.36 – 0.71) and the mean intraobserver kappa coefficient 0.64 (0.42 – 0.87).

6.5 CHAPTER DISCUSSION

The epidemiological characteristics of NHF in the present chapter were very similar to those that were reported in CHAPTER 3. The overall incidence was 72.6 per 100,000 per year and the gender specific incidences were 105.9 and 38.3 per 100,000 per year for females and males respectively. The increase in incidence over the study period in CHAPTER 3 appears to have plateaued. In keeping with the previous literature, males sustained their fractures at a younger age. The vast majority of fractures occurred due to falls from standing height. The incidence of fractures increased with worsening social deprivation.

A novel aspect of the present study was the inclusion of more detailed demographic features such as pre-injury level of function, smoking, alcohol consumption and medical comorbidities. Twenty percent of fractures occurred in smokers, proportionally more of whom were male. Heavy alcohol intake was documented in 23% of patients and also was more common males. Hypertension was the most prevalent medical comorbidity and was present in 138 (33%) patients. Other common medical comorbidities included mental health problems (24%), diabetes (13%) and malignancy (13.%). Liver disease was present in (5%) patients, proportionally more of whom were male.

It is difficult to compare the prevalence of the fracture subtypes in the novel classification with the previous literature as the inclusion criteria for the new subgroups are different than in previously described classifications. Indeed, only 1.58% of fractures were undisplaced according to the new fracture classification, due to the strict criteria that was applied to the undisplaced group. Many fractures that would have been classified by Neer as one-part fell into the lateral compression, early medial separation or medial compression subgroups of the new classification. However, 51% of fractures in the new classification were stable according to the criteria in section 5.3.3 which is similar to the prevalence of one part fractures in previous studies evaluating Neer's classification(1, 33, 64).

Lateral impaction fractures accounted for 22.9% of fractures in the present series. These fractures are similar in morphology to the AO valgus fracture which accounted for 15% of all proximal humeral fractures Court-Brown's series(1). Rather than the true prevalence of these injuries increasing, the discrepancy can be explained by the following reasons. Firstly, isolated tuberosity fractures were excluded from the present series, so as a result of this the proportion of lateral impaction fractures is higher. Secondly, our definition of lateral impaction fracture is similar, but not identical to the AO valgus fracture. We include all fractures with the characteristic anatomical neck fracture and greater tuberosity fracture even if the head angle remains neutral and has not collapsed into valgus as we feel this fracture better considered as part of the spectrum of lateral compression injuries.

In the present series, lateral compression fractures tended to occur in younger patients with fewer medical comorbidities. This is the first study to describe different patient demographics within this fracture subtype.

The early medial separation fracture has not been described previously. In this injury, the medial cortex fails early, resulting in medial translation of the shaft rather than lateral impaction with associated head collapse and fracture of the greater tuberosity that is characteristic of valgus injuries. Patients sustaining early medial separation fractures were older and had more medical comorbidities than those sustain valgus impaction injuries. Differences in bone quality may explain the different fractures morphologies caused by a similar mechanism of injury.

Subtuberosity fractures were seen in 13.8% of patients. This fracture occurs below the surgical neck of humerus but above the level of the humeral diaphysis and is not accounted for in other classifications systems. This fracture was relatively more common in male patients.

Medial compression fractures accounted for almost half of all injuries. 60 percent of these injuries were unstable. Associated displaced fracture of the greater tuberosity was uncommon in stable medial compression fractures but was present in almost half of the unstable fractures.

3.8% of percent of fractures in the present series were unclassifiable. This was a heterogenous group of fractures many of which had their own unique characteristics. No fracture classification can be completely comprehensive and we feel that this small number of unclassifiable fractures is preferable to having a large number of superfluous groups containing very rare fractures. One major criticism of the AO classification is that ten of the 27 different sub-groups listed in the AO classification have an incidence of less than 1%(1).

Three aspects of the new fracture classification were evaluated for interobserver reliability and intraobserver reproducibility. Firstly, assessors were asked to state whether the fracture was 'stable' or 'unstable' according to the criteria in section 5.3.3. Secondly, they were asked to state which broad group the fracture belonged to according to the criteria in section 5.4 (undisplaced, lateral compression, early medial separation, subtuberosity or medial compression). Finally, they were asked to state the fracture subtype according to the criteria in section 5.4.

The level of agreement for fracture stability was 0.67 (substantial) on both inter- and interobserver assessment. The level of agreement for broad fracture group was substantial (0.75) for interobserver assessment and excellent for intraobserver assessment (0.81). The level of agreement for fracture subtype was moderate (0.53) for interobserver assessment and substantial (0.64) for intraobserver assessment.

The level of agreement for fracture subtype in the new classification is similar to the Neer classification. In Sidor's study evaluating the Neer classification, the kappa value was 0.52 for interobserver reliability 0.66 for intraobserver reliability. When the new classification was simplified and assessors were asked to place each fracture into a broad group, both the inter- and intraobserver reliability improved. Sidor did not find a similar improvement to this when they simplified the Neer classification from sixteen categories to six. The five broad groups in the new classification were based on commonly encountered fracture patterns and this, along with the objective criteria that had to be fulfilled for a fracture to be allocated to a group seems to have improved its reliability.

One limitation of the present study is all three of the assessors were orthopaedic surgery registrars and therefore the results may not be generalisable to clinicians from other backgrounds, such as radiologists, consultant trauma surgeons or shoulder specialists. However, it is worth noting that Sidor did include assessors from different backgrounds when evaluating the Neer classification and found no differences in inter- or intraobserver reliability when orthopaedic residents were compared to attendings.

Estimating the sample size required for attaining a particular power for the Cohen's kappa agreement test can be challenging. Numerous methods have been described, including a technique involving simulation, a formula requiring the researcher to estimate asymptomatic variance for kappa and there are studies that provide summary tables showing estimated sample size based on a goodness-of-fit formula but with limited options of the effect size(124). None of these methods provide a definite solution to sample size estimation. A limitation of the present study is that formal sample size calculation was not performed and therefore it may be underpowered. Due to time constraints, only twenty radiographs were evaluated and future studies evaluating larger number would be of benefit.

The fracture subgroups are an important aspect of the new classification despite having poorer inter- and intraobserver reliability than the five broad groups and reliability is only one measure of the usefulness of a classification. For example, simply determining whether a fracture is open or closed would, of course, have excellent reliability. However, grading the soft tissue injury in open fractures may improve clinical decision making but reduce kappa values. Thus, a scheme with more groupings may be less reliable but more prognostic.

The present study had other limitations which should be acknowledged. Firstly, whilst the epidemiology of the fractures is likely to be an accurate reflection of the local population in which the study was conducted it might not be generalisable to all other settings. Data for smoking status, alcohol intake, medical comorbidities and level of independence were obtained from review of the electronic patients record. The electronic patient record contains clinical notes for all patients treated in hospitals in NHS Lothian across all specialties. Whilst it was possible to record smoking status and excess alcohol intake from the electronic patient record, it was not possible to determine the number of cigarettes smoked or the exact volume of alcohol intake for each patient. Additionally, medical comorbidities were only picked up if they were documented on the electronic patient record and it is likely that some patients will have had medical comorbidities that were not documented and that these will have been missed. Prospective data collection using structured proforma might have improved the accuracy of data collection, but it was not possible to do this in the present study due to the very large number of patients.

In addition to nonunion which is evaluated int his chapter, malunion of the tuberosities is an important determinant of functional outcome following NHF. It was not possible to collection functional outcome scores as part of this study but a future study doing so and correlating functional outcome with fracture pattern, in particular tuberosity displacement, would be of use.

In summary, the present study has described the epidemiology of NHF according to the novel fracture classification. The frequency and demographics of each fracture subtype are presented. The data presented in this chapter provides a demographic context for the investigation described in CHAPTER 7.

CHAPTER 7 PROSPECTIVE EVALUATION OF THE NOVEL FRACTURE CLASSIFICATION

7.1 CHAPTER AIMS

The aim of this chapter was to prospectively evaluate the nonunion prediction formula described in CHAPTER 4. The association between smoking, alcohol consumption and medical comorbidities and nonunion was also explored. Finally fracture healing was evaluated in relation to the novel fracture classification described in CHAPTER 5.

7.2 INTRODUCTION

Nonunion of the head to the shaft after NHF is a debilitating complication, historically, the prevalence of which was unclear. In CHAPTER 4, the prevalence of nonunion in following NHF was found to be 7.1%. The radiographic features predictive of nonunion were increasing humeral head-shaft translation, increasing varus angulation of the humeral head, absence of associated tuberosity fracture and separation at the fracture site. Using these four radiographic features, a formula for predicting the risk of nonunion was developed. In addition to these radiographic features, worsening social deprivation was found to be a risk factor for nonunion.

The risk factors and formula for predicting nonunion described in CHAPTER 4 were derived from a retrospective review of a prospectively collected database. The retrospective design facilitated the large sample size which was necessary due to the low prevalence of nonunion, however this methodology does have limitations.

Retrospective studies are open to biases including selection bias and misclassification or information bias. Additionally, with retrospective studies, the temporal relationship can be difficult to assess. Furthermore, it was not possible to study certain patient factors which might have influenced outcome but were not recorded

It was therefore essential to perform a prospective review on a second cohort of patients. The rationale for doing so was firstly to report the prevalence of nonunion in an independent cohort of patients and to validate the predictive formula for nonunion. Additionally, it was possible to collect more detailed information on preinjury level of function, medial comorbidities and smoking and alcohol status which might influence nonunion.

7.3 METHODS

Database 2 was used to evaluate the outcome of humeral neck fractures and then to validate the mathematical model predicting nonunion described in CHAPTER 4. The setting, method of case ascertainment and demographic data collected is described in detail in CHAPTER 2. The following additional data was prospectively recorded by EBG for the purposes of the present study:

7.3.1 **Radiographic data**

All initial post-injury radiographs were prospectively evaluated and the following measurements, that were found to be independently predictive of nonunion on multivariate analysis in CHAPTER 4 were made (a detailed description of the technique used to make the measurements can be found in section 4.3.1):

1. Humeral head-shaft translation
2. Humeral head angle
3. Tuberosity involvement
4. Fracture separation

7.3.2 **Details of primary treatment decision**

The primary treatment decision (nonoperative or operative) was recorded.

7.3.3 **Details of surgery**

Details of primary or secondary surgery (if performed) were recorded. This included the date of surgery, type of surgery, and complications.

7.3.4 Outcome data

Fracture outcome was assessed prospectively. A fracture was judged to be united when a patient had no or minimal pain, no or minimal functional limitation, no mobility at the fracture site, and trabeculation across the fracture on both views or, in those fractures which were displaced, when the lateral bone bridge is complete. Nonunion was judged to be present if there is absence of radiological union and any of ongoing pain, functional limitation or mobility at the fracture site three months following injury.

7.3.5 Mortality data

Mortality data (including verification for death, date of death and cause of death) were checked by anonymised computerised linking with the Regional Death Registry records obtained from the General Registry Office for Scotland. Verification of death and date of death was also cross-checked manually in every patient with electronic hospital records. Survival was assessed from the date of the fracture until the date of death from any cause.

7.3.6 Exclusion criteria

In addition to patients excluded from the epidemiological analysis, the following exclusions were made when evaluating nonunion outcome.

1. Patients who died within three months of sustaining their fracture were excluded deemed ineligible for outcome analysis as they were not at risk of developing nonunion.

2. Patients who underwent primary surgical treatment were excluded from the outcome analysis, as this precluded the natural history of the fracture.
3. Patients with an associated glenohumeral dislocation were excluded as the vast majority of these patients underwent either manipulation under anaestheisia or primary surgical fixation.
4. Patients who defaulted from follow-up within three months of sustaining their fracture whose fracture had not already healed were excluded from the outcome analysis as it was not possible to confirm the presence or absence of fracture union in this group.

7.3.7 **Statistical analysis**

Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington) and SPSS version 21.0 (SPSS, Chicago, Illinois) were used to undertake statistical analysis. Bivariate binary logistic regression was used to estimate the effect of candidate patient- related, injury-related risk and radiographic factors on the development of nonunion. The analysis was performed with independent variables classified as either continuous or categorical data. The relationship of continuous variables with probability of nonunion was examined and tested as either linear or quadratic, depending on whether or not the quadratic term was significant. A linear relationship is a statistical term used to describe a straight-line relationship between a variable and a constant. Linear relationships can be expressed either in a graphical format or as a mathematical equation of the form $y = ax + b$. A quadratic relationship expressed on a graph forms a parabola, which looks like a dip or a valley and the relationship between two variables can be expressed as a mathematical equation of the form $y = ax^2 +bx + c$.

Factors that were significantly predictive of nonunion on bivariate analysis were included in a stepwise multivariate regression analysis (with use of forward conditional methodology) to identify the factors that were independently predictive of nonunion. Factors that were not significantly predictive of nonunion on bivariate analysis were not included in the multivariate analysis. The technique used for the multivariate regression analysis is described in detail in section 4.3.9.

Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability of the model derived from database 1 (CHAPTER 4) to predict nonunion in the patients in database 2. The area under the ROC curve can range from 0.5, indicating a test with no accuracy in distinguishing whether a patient will go onto nonunion, to 1.0 where the test is perfectly accurate in identifying all patients with nonunion. For all of the analyses, a two-tailed *p* value of <0.05 was considered statistically significant.

7.4 RESULTS

Of the 419 fractures included in the epidemiological section of the study, 21 occurred in patients who died within 3 months of injury. These patients were not at risk of nonunion and were therefore ineligible for outcome analysis. This left 398 eligible fractures in patients who survived beyond 3 months of their injury. Post injury radiographs were available for all of these patients. Of the 398 fractures who were eligible for outcome analysis, 31 underwent primary surgical fixation or had an associated glenohumeral dislocation and were therefore excluded. The patient demographics and fracture patterns of those patients that were excluded are summarised in Table 7-1. This left 367 fractures suitable for inclusion in this section of the analysis. Of these 367 fractures 24 either had inadequate radiographs or were lost to follow-up before union was confirmed. Thus 343 out of 367 (93.5%) were included in the analysis.

Patient	Age	Gender	Dislocation	Translation	Head angle	Tuberosity fracture	Separation	Treatment
1	74	F	No	15	170	Yes	No	Surgery
2	73	F	No	21	170	Yes	No	Surgery
3	55	F	No	105	135	No	Yes	Surgery
4	71	F	No	29	139	Yes	No	Surgery
5	66	F	No	3	161	Yes	No	Surgery
6	65	F	Yes	112	85	Yes	No	Nonop
7	87	F	No	124	85	Yes	No	Surgery
8	68	F	No	91	95	Yes	No	Surgery
9	65	M	No	55	135	No	Yes	Surgery
10	44	F	-	-	-	-	-	Surgery
11	52	F	No	5	171	Yes	No	Surgery
12	66	F	No	22	118	Yes	No	Surgery
13	41	M	No	18	163	Yes	No	Surgery
14	66	F	No	6	169	Yes	No	Surgery
15	62	M	No	15	88	Yes	No	Surgery
16	56	F	-	-	-	-	-	Surgery
17	77	F	No	19	125	No	Yes	Surgery
18	62	F	No	126	121	No	Yes	Surgery
19	47	M	Yes	95	90	Yes	No	Surgery
20	54	M	No	15	155	Yes	No	Surgery
21	80	F	Yes	18	95	Yes	No	Surgery
22	87	F	Yes	85	95	Yes	No	Surgery
23	78	F	Yes	21	175	Yes	No	Nonop
24	65	F	No	95	113	No	No	Surgery
25	83	F	Yes	61	94	Yes	No	Surgery
26	59	F	No	22	161	Yes	No	Surgery
27	28	M	Yes	20	150	Yes	No	Surgery
28	46	M	Yes	21	126	Yes	Yes	Surgery
29	63	M	Yes	105	95	Yes	Yes	Nonop
30	45	M	Yes	15	145	Yes	No	Surgery
31	83	F	No	113	92	Yes	Yes	Surgery

Table 7-1 Demographic and fracture characteristics of the patients who either had associated glenohumeral dislocations or underwent primary surgery and therefore were excluded from the analysis. Patients 10 and 16 had their surgery performed at different institutions and their preoperative radiographs were not available for analysis.

7.4.1 Patient demographics

262 fractures (76.4%) occurred in females and 81 fractures (23.6%) occurred in males. The median age of all patients was 71 years (IQr, 60 – 81). The median age of females was 73 years (IQr, 62 – 81). They were significantly older that the males, who had a median age of 66 years (IQr 52 – 18) years; ($p < 0.001$, MWU test).

A good level of premorbid function was noted in the majority of patients with 82.2 percent living independently prior the injury. 90.1% of fractures occurred as a result of low energy injuries.

72 patients were active smokers and 257 were non smokers. Smoking data were incomplete for 14 patients. 81 patients were heavy drinkers and 262 were not.

7.4.2 Prevalence of nonunion

Of the 343 fractures included in the outcome analysis 25 developed nonunion, representing a risk of 7.3 percent (95% confidence interval, 4.6 percent to 10.0 percent).

7.4.3 Age

The median age of patients whose fractures went on to heal was 72 years (IQr, 60 – 81) and the median age of patients whose fracture failed to unite was 69 years (IQr; 55 – 82 years). Age was not predictive of nonunion ($p = 0.741$, Bivariate binary logistic regression).

7.4.4 Gender

7 out of 81 (8.6 percent) males developed nonunion and 18 out of 262 (6.9 percent) females developed nonunion. Gender was not predictive of nonunion on univariate analysis ($p = 0.592$, Bivariate binary logistic regression).

7.4.5 Mode of injury

The mode of injury was not predictive of nonunion on univariate analysis ($p = 0.475$, Bivariate binary logistic regression). Figure 7-1 indicates fracture outcome according to mode of injury.

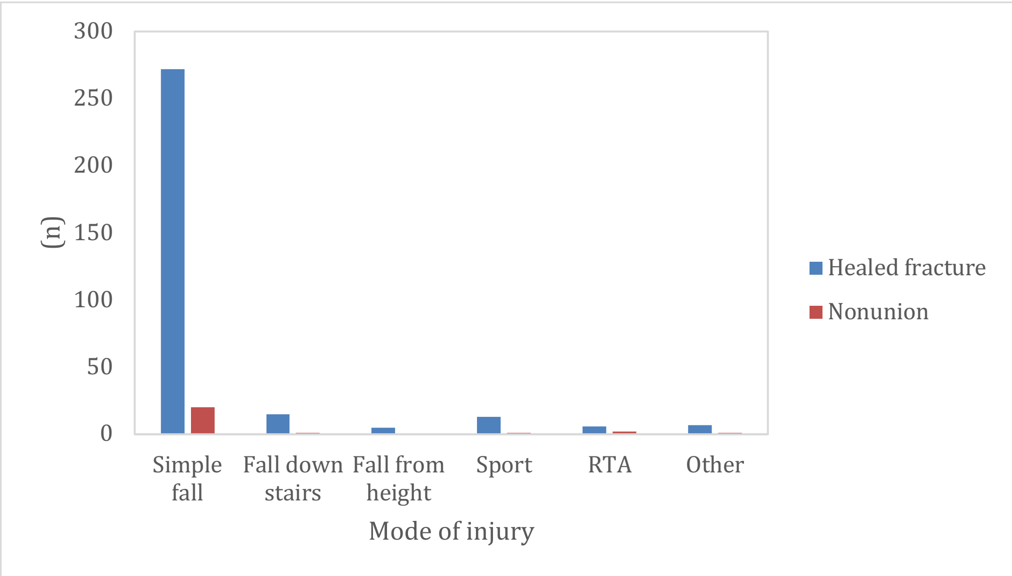


Figure 7-1 Frequency of nonunion according to mode of injury.

7.4.6 Deprivation

The was a trend towards nonunion with worsening social deprivation but this was not statistically significant on univariate analysis ($p = 0.119$, Bivariate binary logistic regression) (Figure 7-2).

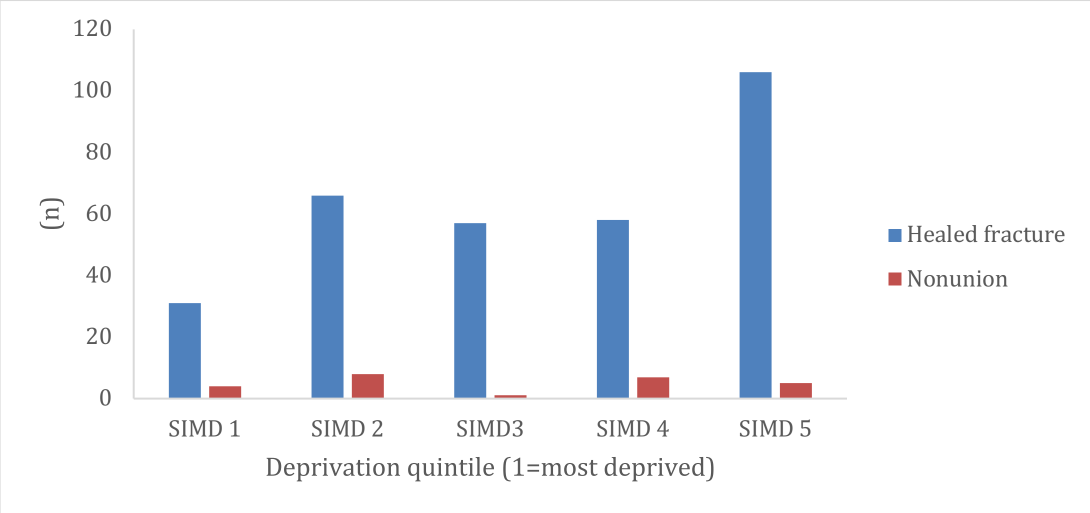


Figure 7-2 Frequency of nonunion according to deprivation quintile.

7.4.7 **Smoking, alcohol and medical comorbidities**

Smoking was predictive of nonunion on univariate analysis ($p<0.001$, Bivariate binary logistic regression) (Table 7-2). Excessive alcohol intake was predictive of nonunion on univariate analysis ($p=0.012$, Bivariate binary logistic regression) (Figure 7-3). The rate of nonunion was 4.4% in non drinkers, rising to 21.1% in excess drinkers. Renal disease was the only medical comorbidity predictive of nonunion on univariate analysis ($p=0.043$, Bivariate binary logistic regression) (Table 7-2).

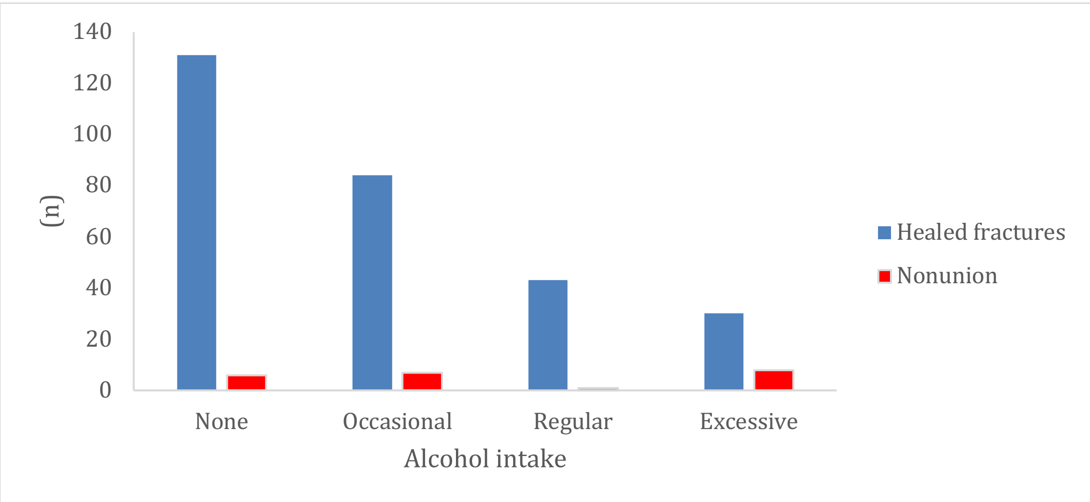


Figure 7-3 Frequency of nonunion according to level of alcohol intake.

Comorbidity	Number of fractures	Number of healed fractures	Number of nonunions	Percentage nonunion (%)	p Value
Smoking	72	59	13	18.1	<0.001
Cardiac disease	61	55	6	9.8	0.401
Respiratory disease	37	33	4	10.8	0.378
Renal disease	26	21	5	19.2	0.043
Liver disease	17	14	3	17.6	0.107
Malignancy	42	40	2	4.8	0.506
Diabetes	56	53	3	5.4	0.863
Hypertension	111	101	10	9	0.399
Stroke	14	12	2	14.3	0.316
Inflammatory joint disease	6	6	0	0	0.999
Mental illness	90	81	9	10	0.253

Table 7-2 Frequency of nonunion according to medical comorbidities.

7.4.8 Multivariate analysis

On multivariate analysis, smoking was the only patient factor that remained independently predictive of nonunion. The regression coefficient B, odds ratio exp(B), and significance are depicted in Table 7-3.

Comorbidity	Regression coefficient (B)	Wald statistic	*p* value of Wald statistic	Standard error of B	Odds ratio Exp (B) (95% CI)
Smoking	1.737	13.881	<0.001	0.466	5.697 (2.278-14.160)

Table 7-3 Multivariate analysis.

7.4.9 **Prospective validation of non-union model**

The formula derived from database 1 was predictive of nonunion when applied to database 2 ($p<0.001$, Bivariate binary logistic regression). The area under the receiver operating characteristic curve was 0.882 (good). In comparison, the area under the curve was 0.921 for the analysis of database one, suggesting the values in Table 4-4 and Table 4-5 were only slightly over optimistic.

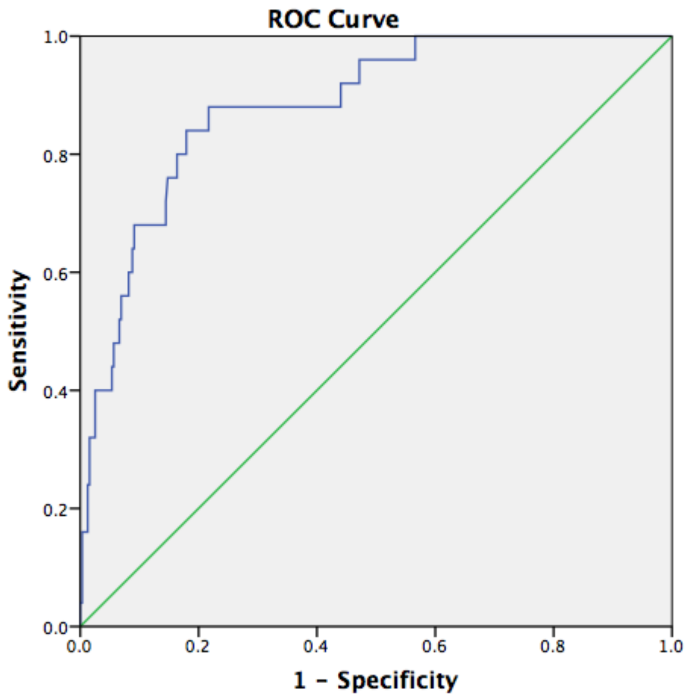


Figure 7-4 Receiver operating characteristic curve for the logistic regression model.

7.4.10 **Nonunion risk by fracture subtype**

The rate of nonunion in each of the fracture subtypes is shown in Table 7-4.

Fracture subtype	Number of fractures (%)	Number healed	Number nonunion
Undisplaced			
UD (61)	8 (2.3)	8 (100)	0 (0)
Lateral compression	87 (25.4)		
LC1 (21)	36 (10.5)	36 (100)	0 (0)
LC2 (22)	33 (9.6)	33 (100)	0 (0)
LC3 (24)	18 (5.2)	18 (100)	0 (0)
EMS	31 (9.0)		
EMS1 (26)	27 (7.9)	27 (100)	0 (0)
EMS2 (23)	4 (1.2)	4 (100)	0 (0)
Medial compression	165 (48.1)		
MC1 (32)	69 (20.1)	68 (98.6)	1 (1.4)
MC2 (322)	5 (1.5)	5 (100)	0 (0)
MC3 (33)	30 (8.7)	26 (86.7)	4 (13.3)
MC4 (34)	11 (3.2)	11 (100)	0 (0)
MC5 (35)	29 (8.5)	21 (72.4)	8 (27.6)
MC6 (36)	21 (6.1)	17 (81.0)	4 (19.0)
Subtuberosity	47 (13.7)		
ST1 (42)	26 (7.6)	22 (84.6)	4 (15.4)
ST2 (43)	21 (6.1)	17 (81.0)	4 (19.0)
All stable	196 (57.1)	195 (99.5)	1 (0.5)
All unstable	142 (41.4)	118 (83.1)	24 (16.9)
Fracture dislocation			
FD (50)	5 (1.5)	5 (100)	0 (0)
Total	**343 (100)**	**318 (92.7)**	**25 (7.3)**

Table 7-4 Nonunion risk according to fracture subtype.

7.4.11 Smoking and radiographic predictors of nonunion

When smoking was assessed alongside the prediction formula derived from database one, both were independently predictive of nonunion. The regression coefficient B, odds ratio exp(B), and significance for each variable used for estimating the risk of non-union in the final model are depicted in Table 7-5.

Comorbidity	Regression coefficient (B)	Wald statistic	*p* value of Wald statistic	Standard error of B	Odds ratio Exp (B) (95% CI)
Prediction formula	0.072	27.317	<0.001	0.014	1.075 (1.046-1.104)
Smoking	1.873	12.715	<0.001	0.525	6.506 (2.324-18.211)

Table 7-5 Multivariate analysis.

7.5 CHAPTER DISCUSSION

Of the 343 fractures included in the outcome analysis 25 developed nonunion, representing a risk of 7.3 percent. The formula developed in CHAPTER 4 was predictive of nonunion in this independent, prospectively collected database. Receiver operating characteristic curve analysis showed good performance of the predictive model. Smoking was the only patient factor that was independently predictive of nonunion on multivariate analysis. According to the novel classification, 24 nonunions occurred in unstable fractures and only one stable fracture developed a nonunion.

The rate of nonunion in the present chapter was similar to that reported in CHAPTER 4 (7.3% and 7.1% respectively). It is likely that the true rate is slightly higher than this as a small proportion of patients with more severe injuries in both series were excluded as they underwent primary fixation Certainly, the rate of nonunion appears to be higher than 1.1% which was reported in the only previous similar study to this(3).

The prediction model described in CHAPTER 4 performed well when evaluated when evaluated against the prospectively collected database. The area under the curve on the receiver operating characteristic curve analysis was only slightly smaller than what was found in CHAPTER 4 however the performance of the model was still 'good'. This suggests that the four radiographic risk factors for nonunion that were identified in CHAPTER 4 appear to be valid.

The results of this study suggest that smoking plays an important role in the development of nonunion after NHF. Over 18% of smokers had fractures that did not heal and when smoking status was evaluated alongside the radiographic predictive formula, it remained independently predictive of nonunion. The increased risk of nonunion in patients from lower deprivation quintiles that was reported in CHAPTER 4 may have been due to the fact that cigarette smoking is more common in patients from more deprived residential areas(125).

It would appear that the risk factors for nonunion are multifactorial, with host factors (ie smoking) and mechanical factors (ie fracture morphology) playing a role. This is in keeping with a previous study that divided the causes of nonunion were divided into four categories: mechanical; infection; dead bone with a gap; and host. The majority of patients with nonunions were found to have two causative factors of which mechanical (59%) and host (43%) factors were common causes(126). Smokers with radiographic risk factors for nonunion should be counselled regarding the risk of nonunion. Excess alcohol excess was predictive of nonunion on univariate analysis but was on multivariate analysis. Alcohol excess appears to be a confounding factor as many patients who drink excess alcohol are also cigarette smokers which appears to be the causative factor of their nonunion.

Using the novel fracture classification, only one patient out of 195 (0.5%) with a stable fracture developed a nonunion. Patients with stable fractures can be reassured that their fracture is likely to heal, and they may not require long term follow-up or serial radiographs which might reduce unnecessary radiation exposure and allow healthcare cost savings. 24 patients with unstable fractures developed nonunion. Patients with unstable fracture patterns should be carefully followed up to fracture union. Further prospective randomised trials would be of use in patients with unstable fractures to evaluate the role of primary surgery in this group.

CHAPTER 8
CONCLUSIONS

The study on epidemiology of NHF (CHAPTER 3) demonstrated an association with fragility and highlighted the importance of non-operative treatment for the majority of these injuries. Given the number of elderly patients sustaining these injuries, consideration of osteoporosis is also important and future work is needed to determine the role of bone quality following these fractures, particularly in post-menopausal women.

The rate of nonunion following NHF was found to be 7.1% in CHAPTER 4 and 7.3% in CHAPTER 7. Cigarette smoking was found to be independently predictive of nonunion. The independent radiographic predictors were increasing translation of the humeral shaft in relation to the humeral head, increasing varus angulation of the head, absence of tuberosity fracture and separation at the fracture site.

A novel fracture classification was described in CHAPTER 5. Fractures were classified according to mechanism failure and stability based on the radiographic risk factors described in CHAPTER 4. This classification was found to have good interobserver reliability and intraobserver reproducibility. Further epidemiological analysis found that the majority of fractures were stable according to the novel classification emphasising the role of non-operative management in these patients. There were however a proportion of patients with unstable fractures and prospective analysis found that the rate of nonunion approached 20% in this group. Prospective evaluation showed that the risk of nonunion was almost negligible in stable fracture but was much higher in unstable fractures.

Further large prospective randomised trials focused on high functioning patients with high risk fracture subtypes according to the novel classification are essential to make definitive conclusions about the role of operative treatment for these injuries.

CHAPTER 9
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